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THE AMERICAN
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EDITORIAL

MILK IS generally regarded as a perfect food. Obviously, through the influence of many centuries of evolution it has become adapted to the nourishment of the growing infant among all nursing animals. Bunge asserted many years ago that it is somewhat deficient in iron, but clinical experience does not seem to have confirmed this view as of serious practical value. That it is well adapted to the nutritive requirements of the growing infant is fully sustained by experience. Up to a recent period attention was directed to its more marked chemical and physical characteristics. It contains fat in a peculiar condition eminently fitted for digestion and its nitrogenous constituents are also in a special labile form. It is now known that the fat contains minute amounts of a substance that has great influence on nutrition and is necessary to the satisfactory use of the milk. This "fat-soluble" or "vitamin A" has been extensively studied in feeding experiments.

Milk being largely eaten raw, commercial milks have been the subject of extensive study by sanitarians, and all civilized states have regulated the sale by establishing standards of chemical composition, and other data. In the early days of this regulation, which was in the main developed by the British Society of Public Analysts, the chemical composition was alone considered, the object being to detect the two most common departures from proper quality, skimming and watering. Bacteriology had not been brought to practical application, and hence the first standards of milk were simply the fat and solids-

not-fat. In a few cases, notably that of one of Dairy Companies of London, to which Mr. H. Droop Richmond was chemist for many years, the supervision covered the general condition of the farms from which the milk was obtained.

Many changes have come over the problem of milk supply in the last score of years. The introduction of the tuberculin testing of cows, the knowledge of the readiness with which some diseases may be transmitted and the recognition of the liability to contamination by ordinary microbes in the handling of milk, have all called for elaborate organization to secure safety to the public at large, for milk is extensively consumed raw and, therefore, the microbic and enzymic contents are active.

To reduce the danger of contamination at source and in transit, pasteurization is now largely employed, the bulk of the milk served in bottles being thus treated. It is a question how far such treatment diminishes the nutritive value of the product. There are both clinical and chemical data to show that some damage is done to milk in the commercial pasteurization.

Specific clinical evidence is found in a paper by Drs. Ladd, Evarts and Franks, printed in the *Archives of Pediatrics* for July, 1926, a reprint of which has been issued. The conclusions are supported by an extended and careful investigation among babies in the care of the Boston Dispensary, an organization through which is supervised the health of children who are wards of the Boston Children's Aid Association and the Church Home Society. Many of these infants remain under care for several years and their condition can be well observed. The conclusions are stated as follows:

It is apparent from these observations that only a very small percentage of babies fed on raw certified milk (without orange juice or cod liver oil) developed even mild X-ray rhachitis of the wrists. These cases (18 per cent. of the number observed) were healing or healed at the end of the period of observation.

Cases mildly rhachitic (by X-ray) at the beginning showed healing or healed processes at the end of the period of observation, with-

out supplementary doses of orange juice or cod liver oil. The protection and healing properties of the certified milk on rhachitic processes was clearly evident.

The group of babies fed on grade A pasteurized milk showed a greater incidence of X-ray rhachitis at the beginning of observation, that is, 66 per cent., but with cod liver oil and orange juice, were, without exception, healing or healed at the end.

In addition it is worth noting that experiments made by the present writer show that the test for distinguishing between raw and boiled milk indicates that some reactive enzyms are seriously injured by the heating required for pasteurization. The test most usually employed is an addition of benzidine hydrochloride and hydrogen peroxide. Raw milk produces a bright blue tint, but sterilized (boiled) milk gives no color. When the test is applied to the milk supplied to the household only a faint color or sometimes none is obtained. This fact would indicate that the lack of nutritive value in the pasteurized milk is due to some change in the enzym content, and these may be of much importance in the dietetic value of the food.

It is also worth noting that milk contains a large amount of calcium salts. These are absolutely necessary to the growing infant, but it is a question whether such a diet is suitable for persons beyond middle age in whom there is less need of calcium. A large proportion of urinary calculi are calcium oxalate, one of the hardest forms and one which the general principles of therapeutics do not seem to afford any remedy. It would seem to be a reasonable rule that the ingestion calcium salts should be low in the later periods of life, and this might be applicable to the composition of the water used as well as to the food. There is at present an effort on the part of certain purveyors of natural waters to condemn distilled water as unwholesome, but there appears to be no chemical or physiologic information to that effect.

HENRY LEFFMANN.

ORIGINAL ARTICLES

EPOCHS AND EPOCH MAKERS OF MEDICINE*

Horatio C. Wood, Jr., M. D.

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THE WORD epoch is often applied, somewhat loosely, to any event of more than ordinary importance in the development of a science. With such a definition the title of this lecture would become ridiculous because even a mere list of the great discoveries of medicine could not be confined within the limits of a single lecture. I use the word, however, in the stricter meaning of "an event in the progress of history from which succeeding years are counted."

Horatio C. Wood, Jr., M. D.

From a medical viewpoint the 30 centuries of history divide themselves, almost naturally, into five eras which may be approximately dated as follows:

1. Sacerdotal or Premedical, from dawn of history to 200 B. C.
2. Speculative Medicine, from 400 B. C. to 200 A. D.
3. Dogmatic Medicine, from 200 to 1600 A. D.
4. Early Scientific Medicine, from 1600 to 1850.
5. Modern Medicine, from 1850 to present time.

Practically all races of primitive peoples have attributed disease to the machinations of evil spirits. It is only natural, therefore, that in the early periods of civilization treatment of the sick should have been in the hands of the priesthood. At first this duty appears to have been assigned indiscriminately to any member of the sacerdotal class, but when civilization began to become more complex, there was manifest a tendency towards specialization, and distinct groups of priests were especially charged with the exorcism of the demons of disease. Thus, among the ancient Greeks this function belonged to the priests of Aesculapius, the son of Apollo; while in Egypt it

*One of a Series of Popular Science Lectures given at the Philadelphia College of Pharmacy and Science, 1926-27 Season.

was assigned to those who were consecrated to the worship of Osiris.

Gradually, by the accumulation of experience, these groups of priests acquired some knowledge of the beneficial effects of material agencies, such as certain herbs, as an aid to the religious ceremonies which were the important part of their treatment.

It seems probable that Moses acquired the knowledge of hygiene which is so manifest in the laws that he gave to the children of Israel from his early training as a priest of Osiris.

HIPPOCRATIC ERA

The Greeks were never a people of strong religious instinct, and, despite the wealth of imagination shown in their theological myths, they do not appear to have taken their religion with the same seriousness as, for example, did the Semitic peoples. It is not surprising, therefore, that comparatively early in Grecian development there grew up a guild of medical practitioners—called Asclepiadæ—who were not members of the priestly class, although they did mix more or less theurgic therapy with their drugs. The most famous of this group was Hippocrates II, commonly called "The Great." He was born about 460 B. C., one of a long line of hereditary practitioners of the healing art. Recognized even by his contemporaries as an intellectual giant, he exerted a most potent and salutary influence on medical thought; so much so, that he is commonly referred to as "The Father of Medicine." While not the first physician whose name has come down to us, he nevertheless deserves the title because, more than any other single man, he was responsible for the establishment of the medical art by rescuing it from the shackles of priestly superstition.

Hippocrates and his contemporaries bothered themselves but little with what we now call the medical sciences. He observed and reported on the manifestations or symptoms of disease, theorizing on their prognostic importance, but displays very little curiosity as to the mode of their production. He made some anatomical studies, but of physiology he remains almost completely silent. His great contribution to medicine was the doctrine, still held today, that the art of medicine should be based on observation and reasoning from experience, rather than the application of theories evolved from the inner consciousness.

In the centuries immediately succeeding Hippocrates, largely under the influence of philosophers like Plato and Aristotle, physi-

cians began to interest themselves in how the body functions, but their ideas were derived from conjecture rather than observation. The result of this method was an extraordinary diversity of opinion and the consequent formation of a large number of "schools" of medical practice.

Long after Greece had lost her political supremacy she still retained her intellectual dominance; for the science, like the art, of Rome was largely a borrowed culture. The post-hippocratic era of speculative medicine lasted through the rise and decline of Grecian greatness and about the time of the height of the Roman glory underwent a sort of crystallization, the taking on of a fixed form. This change was largely due to one man who, like so many of the Roman physicians of the time, was of Greek extraction.

GALENIC ERA

The foremost character produced in this period was Claudius Galen. Born 141 A. D., in the city of Pergamus in Asia Minor, he was thoroughly educated both in the humanities and in the medical lore of his day, first at his native town, then in Smyrna and finally at Alexandria, where gathered the most famous teachers of ancient times. At the age of 34 he went to Rome, where he resided for the remainder of his life, save for the time spent in traveling. Here he acquired such fame that he was invited by the Emperor Marcus Aurelius to accompany him in one of his military expeditions, an invitation which he declined.

Galen was a most versatile and prolific writer, with a supreme confidence in his own judgment and a consequent contempt for those who differed with him. He did considerable real investigation in anatomy but even here did not hesitate to surmise what he could not see. His physiological and pathological writings, while voluminous, seem to be founded more on what he thought ought to be than on what really is.

During his lifetime, and for some years after, Galen had many opponents, but as Europe gradually sank into the mental stagnation of the dark ages his writings came more and more to be regarded almost in the light of divine revelation and for more than a thousand years completely dominated medical thought.

The same spirit held the scientists then as now governs so many of our theologians. Authority, not reason, was the guide men followed. To doubt the teachings of the medical classics, such as the writings of Galen, was to court both scientific and social ostracism,

and few there were with sufficient temerity to undertake the task of attacking theory with fact. The conditions which made an intellectual martyr of Gallileo and cast Roger Bacon into prison, do not create an atmosphere in which science is likely to flourish.

The progress of the art of medicine must always be largely conditioned on the status of its fundamental sciences. The current hypotheses concerning bodily functions in health and the causes of the deviations from the normal which we call disease, must, to a large extent, determine the accepted method of treatment. When physiology is based upon a collection of fancies instead of an aggregation of facts, no great advance may be expected; a polluted fount does not give rise to a healthful stream. Small wonder that by the Middle Ages the healing art had reached a stage of arrested development. When to ask a question was to commit a crime, no progress was possible. The intellectual renaissance, which occurred about the time of the discovery of America, was slow to affect medical thought. While from the New World there came a few valuable drugs, and there was real progress in the treatment of one or two diseases, notably malaria fever, as a whole the fifteenth century represents the blackest period of medical ignorance.

But the night is the darkest before the dawn, and, in the year 1578 there was born in England one who was destined to give a new birth both to medical science and practice. If Hippocrates deserves the title of "Father of Medicine," then William Harvey may justly claim the distinction of "Father of Modern Medicine," for it was on his solution of the incomprehensible problem of the circulation of the blood that is founded the pillar on which rests all our present concepts of physiology.

In order to understand the revolutionary nature of the ideas put forth by Harvey, it is necessary to briefly review the current tenets concerning the distribution of the blood which were, with only slight modification, those taught by Galen.

It is scarcely accurate to speak of Galen's theory of the circulation of the blood because he had no concept of a continuous flow in a circle, which is the basic idea conveyed by the term circulation. While it is difficult to apprehend all the details of his notion, in a general way it seems to have been about as follows: There are two sorts of blood in the body, one carrying the grosser, nutritive, elements to the tissues; the other supplying "vital spirits." The nutritive blood is manufactured in the liver from the digested food received from

the intestines; it is distributed through the veins to various parts of the body. The veins start from the liver and run to all the organs including the lungs and the heart. He likens this system of distribution to the irrigating canals in a garden and calls attention to a wonderful provision of nature by which the different organs "should neither lack a sufficient quantity nor be overloaded at any time with an excessive supply"; obviously there is nothing here to suggest any idea of a circulation.

The vital spirit (apparently a similar concept to the "breath of life" used in the Bible) is concocted in the heart from the air taken into the lungs. The heart by its dilation draws the air and blood from the lungs; he says "as the bellows of a blacksmith draw in air when they expand, as the flame of the lamp draws oil through the wick, or as the magnet attracts iron, so it is with the heart; it possesses in itself an inherent power of attraction." The vitalized blood is carried to the distant parts by the arteries, which by a similar expansion suck the blood from the heart. As his anatomical observations had shown him that the artery from the lungs runs to the right side of the heart, while that going to the rest of the body comes from the left side, it was necessary to explain how the blood gets from the right to the left heart. This he did by imagining the existence of minute openings in the septum—or wall between the two cardiac chambers (see Fig. 2).

Galen believed that the blood running to the various organs was just enough to fulfill their nutritional requirements and that it, all of it, whether the venous blood or the vital spirits, was consumed by the tissues; he had no idea of any return flow either to the heart or to the lungs.

The Galenic dogmas were accepted, almost without question, for more than 1300 years, but towards the end of the sixteenth century anatomists began to realize that there were certain facts which could not be explained by his theory. In 1543 Andreas Vesalius, then Professor of Anatomy at the great University of Padua, published a book on the anatomy of the heart in which he stated that he could not see any openings through the septum; while it seems apparent that he did not believe there were any, he did not have the courage to actually deny the doctrine, in the face of its universal acceptance, but merely says that he is "in great doubt as to this function of the heart."

At this time there was living a man, named Michael Servetus, remarkable for his heretical character, both theologically and medically. How extraordinarily heterodox he was is suggested by the fact that he was condemned to death by the followers both of the Pope and of John Calvin. The latter, however, had the advantage of possessing his body and actually burned him at the stake, while the papal party were perforce satisfied with burning his effigy. In one of his theological disquisitions—for it must be remembered that men then mixed their theology and medicine in a manner which seems to us today to be strangely naïve—Servetus showed that there really were no openings in the septum between the two sides of the heart, and that Galen's explanation of how the blood got from the right to the left heart was evidently untenable. This was one of the sins for which he paid with his life. He maintained that the blood, to get from the right side of the heart to the left, must pass through the lungs, a view which we today know is correct. He did not appear, however, to have any notion of a continuous flow in a circle, that is circulation. Moreover, as all his books, which could be found, were burned with him in 1553, his doctrines had little effect upon general opinion.

It is possible, however, that they bore fruit through their influence on Colombo. The latter, originally an apothecary, took up the study of medicine and became first assistant and then successor to Vesalius. In a posthumous work, published in 1559, he categorically denies the possibility of blood passing through the cardiac septum and clearly intimates some idea of a pulmonary circulation. He accepted, however, the rest of the theory of Galen.

HARVEIAN ERA

Such was the general status in the year 1578, when William Harvey was born. He was the son of a man of some local importance who had been successively Alderman and Mayor of Folkestone. His early education was received at an institution, of which he later became the most powerful patron, called Caius College. Subsequently, he went to the University of Cambridge, and from there to Padua in Italy, which was at that time the most famous seat of medical learning in the world.

In 1602 he returned to England to engage in the practice of medicine, and became Professor of Anatomy in the College of Physicians in 1615. Three years later he was appointed Physician Extraordinary to the Court of King James, and later became the personal

physician and friend of the unfortunate son of that monarch known in history as Charles I.

After the overthrow of the royal power by Cromwell, being then a man well on towards seventy years and afflicted with gout, he retired from public life and lived with his brothers, who were successful merchants in London, where he died of apoplexy in his eightieth year.

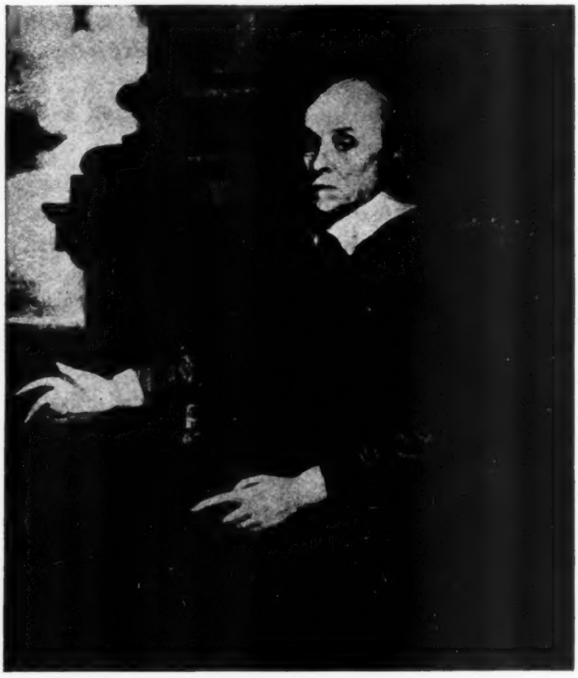
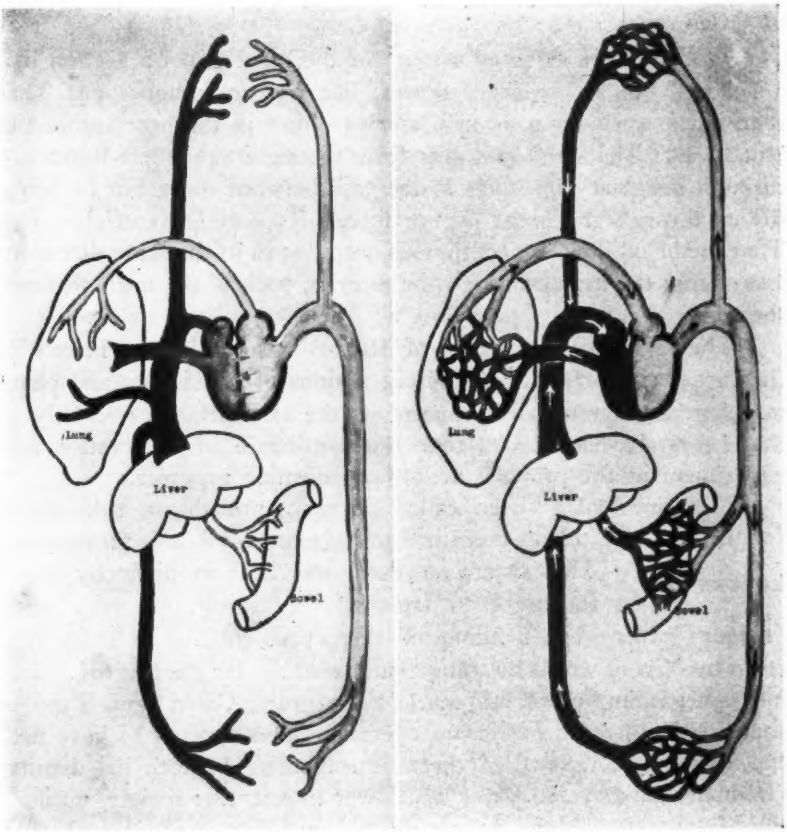


FIG. 1
William Harvey

There is strong evidence that Harvey taught his students the novel doctrine of the circulation of the blood almost from the beginning of his work as Professor of Anatomy, but it was not until 1628 that he made public his heretical and revolutionizing theory in a pamphlet that was printed in Germany at Frankfort-on-the-Main. Perhaps the intervening dozen years had been used by him to further assure himself of the correctness of his views, but it seems to me more probable that the delay was due to his recognition of the storm

of criticism and vilification which was sure to follow such an impious flouting of the authority of the ancients; by 1628 he was established, not only as a successful practitioner and respected teacher, but



A. **B.**

FIG. 2

A. Galen's concept of the distribution of the Blood. The nutritive blood comes from the Liver and is carried through the body by the veins; the "vital spirit" comes from the heart and is distributed through the arteries.

B. Harvey's theory of the circulation of the Blood. There is only one kind of blood, which is pumped by the heart, through the arteries, to the body and back through the veins, to the heart.

also as a favorite intimate of royalty. Among the more kindly explanations of his conduct which were offered by his orthodox antagonists, was that he was demented. While in view of his profes-

sional and political prominence, these attacks did not altogether destroy his position in England, they did cause the loss of a great part of his private practice, which he seems never to have regained.

The fundamental differences of the Harveian concept from that of Galen are:

(1) That the essential activity of the heart is not a suction like a bellows, but an expellant power, like a force pump. (2) That there is no such thing as vital spirits, either in the heart or in the blood. (3) That the blood gets from the right to the left heart, not through imaginary openings in the wall between them, but by being driven through the lungs by the force of the right ventricle. (4) That the blood flow is a continuous one, always in the same direction, away from the heart, through the arteries, back to the heart through the veins.

The supreme significance of Harvey's work lies not merely in the fact that nearly all our present notions of physiology and pharmacology are built on his concept of the circulation, but chiefly in that he established for all time the dominance of observation and experiment as the primary factors of scientific progress.

Medicine had a sister, called Surgery; probably a twin sister, for the ancient Asclepiads seemed to have practiced both professions.

MODERN ERA

This sister, however, was held in distinctly lower esteem, even from the beginning; the very word "surgery" conveys something of disparagement for it is derived from two Greek words meaning "hand work." By the time of Galen, it was beginning to fall into marked disrepute. Galen himself makes some slight mention of certain operations, but appears to have held the actual performance of them as something beneath his dignity. Gradually surgery fell lower and lower in scientific society, until, in the Middle Ages, it was largely given over by the medical profession to the tonsorial profession.

When one considers the conditions under which operations were performed, it is not to be wondered at that men of fine sensibilities wanted little to do with it. Imagine the poor victim, held to the table by several stalwart assistants, while the barber-surgeon went ahead with his cutting and sawing, amid the pitiable shrieks and writhings of the suffering patient. When the cutting was over, the wound was seared with a red-hot iron or boiling oil. After this torture there remained a long and painful period of convalescence. Let me read a quotation from a letter, written by a physician to the great English

surgeon John Hunter, towards the end of the eighteenth century. This physician, for some reason, required an amputation of his leg, and from it he learned how operations were viewed by the patient. A part of his letter is as follows:

> "Of the agony occasioned, I will say nothing. Suffering so great as I underwent cannot be expressed in words. . . . But the black whirlwind of emotion, the horror of great darkness and the sense of desertion by God and man, bordering close on despair, I can never forget however gladly I would do so. . . . I still recall with unwelcome vividness the twisting of the tourniquet; the first incision; the fingering of the sawed bone; the sponge pressed on the flap; the stitching of the skin." *

In an address before the American Surgical Society, the late Dr. Warren of Boston, said of the suffering of the convalescent period:

> "The dread of pain was not confined to the operation, for in the early days, the after treatment was of the most torturing description. Every flap of skin, instead of being re-united, was cut away; every open wound was dressed as a sore, and every deep one plugged up with a tent, lest it should heal. Long tents were thrust into the wounds of the neck and cheek until the neck and head swelled enormously."

Life itself was almost too dearly purchased at such a price, and it is small wonder that patients not infrequently committed suicide rather than endure the horrors of an operation.

The tortures of the operating room were greatly mitigated by the introduction of surgical anæsthesia in 1847, but the sufferings of the convalescent period and the frightful mortality which followed surgical interference were not materially affected by this great boon. In the very best hospitals of Europe, after simple amputations, from forty per cent. and upwards of the patients died from the operation; one of the surgeons in Napoleon's army, Dr. Faure, reports that after the Battle of Fontenoy of three hundred amputations performed, only thirty patients survived. The great majority of these deaths were due to gangrene and other types of wound infections, which the surgeons were powerless to prevent or relieve because of their complete ignorance of their source.

The year 1927 marks the centennial of the birth of the man who blazed the way for prevention of wound infections and made pos-

*Quoted from Ashhurst, *Internat. Med. Mag.*, October, 1896.

sible modern surgery. Himself a practical surgeon, with large experience, his work was so intimately mingled with, and dependent on, the investigations of a group of laboratory scientists that it savors of unjust discrimination to single out any one man as deserving of the glory of originating what is commonly called the germ theory of disease.

The beginning of this great discovery, which marks the opening of the era of modern medicine, had its roots back in the seventeenth century. As a preliminary necessity for the discovery of bacteria and their relation to disease was the compound microscope, for without this instrument it is obviously impossible to see those minute particles of living matter; so small are they that half a million of them would scarcely cover the head of a common pin. Probably the first man ever to see a bacterium was the Dutch dilettante scientist Anton Van Leeuwenhoeck, sometimes called the "Father of Microscopy," although not the inventor of the microscope. Although after he described these minute forms of life, they were the subject of much scientific curiosity and study, interest in them was purely academic and was confined for one hundred and fifty years almost exclusively to botanists.

At this stage there appears on the scene a French chemist, whose interest in the properties of the different forms of tartaric acid eventually led him to show that vinous fermentation was due to living organisms closely related to these botanic curiosities.

Louis J. Pasteur was born in the town of Dôle, in Eastern France, the son of a tanner, in the year 1822. He never studied medicine, but became Professor of Chemistry in the University of Strassburg in 1856, and subsequently at the Sorbonne in Paris. The year of his entrance into Strassburg is also noteworthy for the beginning of a series of publications dealing with the cause of the change of grape juice into wine and the subsequent spoiling and souring of the wine. He showed that these changes were due to the presence of microscopic vegetables, and that if the wine were heated it would keep indefinitely. He did not give any attention to the possibility of connecting these organisms with disease of either man or beast until after the work of one of his contemporaries had made such a hypothesis probable. Although not the originator, therefore, of the germ theory of disease, he subsequently made very valuable contributions to the development and establishment of this theory. He died

in the year 1895, rich in the honors bestowed by his country and the world-wide recognition of a grateful humanity.

The first investigator to assign to bacteria a definite role in the causation of a disease appears to have been Casimir Joseph Davaine, who was born in Saint Amand-les-Eaux, a village of Northern France whose hot springs were famous in the time of the Roman invasion. He graduated in medicine in Paris in 1837, but devoted his life chiefly to scientific research. In 1855 he described a peculiar microscopic rod-shaped body, which he found in the blood of sheep that had died of anthrax. At first he attached no significance to these corpuscles, but after the publication of Pasteur's work on the fermentation of wines the similarity in appearance of the growths described by Pasteur with those he had observed in anthrax suggested to his fertile mind the possibility of a causal relationship, and he undertook some experiments to determine the truth of this theory. In 1863 he published the results of experiments from which he drew the conclusion that these rod-shaped bacteria were the cause of that terrible plague, which has been, and still is, of such great economic importance in agricultural regions. This thought was almost as startling as would be the suggestion today that gravitational attraction was due to bacteria. It is not surprising, therefore, that the evidence he adduced in favor of his theory was not held sufficient by his contemporaries to justify its acceptance; and it was not until the German bacteriologist Robert Koch, by his more exacting methods, had demonstrated the truth of Davaine's hypothesis, that it was generally accepted.

While these revolutionizing ideas were exciting the scientific circles of France and Germany, an English surgeon was applying the work of these laboratory investigators to the practical benefit of humanity. As the centenary of his birth is so near at hand, I have thought it only just to speak a little more at length, both on the man and his achievements.

Joseph Lister was born of Quaker lineage, in the town of Upton, in Essex, England, April 5th, 1827. He was a gentle, kindly man, as widely loved for his attractive character as he was esteemed for his professional attainments. Fielding Garrison, in his *History of Medicine,* says of him: "The character of Lister is one of rare nobility. As the Quaker is the Puritan transposed into a softer and more grateful

key, so his nature had those elements of sweetness which probably can come only out of strength." *

In 1860 Lister became Professor of Surgery in the University of Glasgow, and from then until his death in 1912 was universally regarded as one of the foremost surgeons of England. To a man of

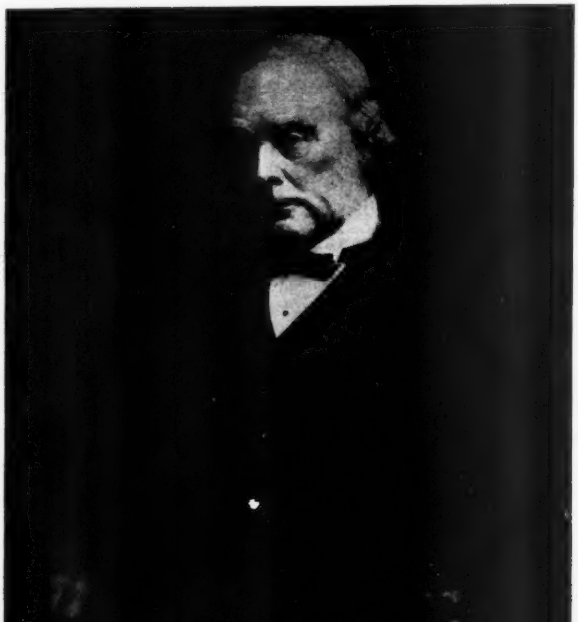


FIG. 3

Joseph Lister

his sympathetic character, the sight of the suffering in the Surgical Ward was a source of continual torment; intuitively he felt that there must be some way out of this maze of death and suffering. When he heard, in 1864, of Pasteur's discovery that sterilization of wine prevented its spoiling, the thought immediately came to his mind

**History of Medicine*, 1921.

whether some analogous principle might not apply to wounds. Obviously one could not sterilize the seat of an operation by boiling the part, and so he turned to chemical substances which were known to destroy bacteria. After experimenting with several of these, he finally decided on carbolic acid as the most available disinfectant for the purpose. The technique as at first developed by him, called for a continuous spray of a solution of carbolic acid over patient, operator and instruments. The first operation under this technique was performed in 1865, and the first publication of his results showed a reduction in the mortality of his own operations to about one-fourth of their previous number.

Like all innovations, his theories and methods had their detractors, but the work of Davaine, of Koch and of Pasteur had prepared the minds of the scientific world, and soon, as reports from other surgeons of similar successes under the Lister technique came pouring in, the medical world was shaken as by a hurricane, and when Lister visited Germany, in 1880, his travel was like the triumphant tour of a conqueror. He was a conqueror, greater than Alexander or Cæsar or Napoleon. Where these have left in their wake thousands of corpses, Lister's pathway is marked with hordes of living men and women. His native land recognized his achievements with a title of nobility; the only instance, I believe, where an English physician has been elevated to the peerage. Learned societies and institutions bestowed upon him all sorts of honors and degrees; and he lived to hear the unending plaudits of a grateful humanity and to realize that thousands upon thousands, yet unborn, were to owe their lives to his discovery.

The germ theory of disease is of no less importance to medicine than it is to surgery. Diphtheria, the dread scourge of childhood, was conquered years ago and the day is not far distant when it will be exterminated from the earth. Within the last few years a similar power has apparently been acquired over scarlet fever. Yellow fever, which, a few years ago, numbered its victims by the thousands, is a thing of the past. The Black Plague of medieval Europe which according to LaWall * caused in the thirteenth and fourteenth centuries the death of sixty million persons, is still endemic in Asia; but Europeans and Americans, by their knowledge of bacteriology are able to protect themselves against its ravages. Pneumonia and influenza, and

**Four Thousand Years of Pharmacy*, 1927, p. 148.

a few other diseases still remain to be subdued, but I surmise that they too, in the not remote future, shall yield to our growing knowledge, and only gunmen and automobiles will be left to bring us to untimely graves.

What of the future? We of today are wont to look back on the practices of the ancients with mingled scorn and amusement but we may well take to ourselves the words of the prophet Elijah: "I am not better than my fathers." Let us not forget that we are building on the foundations they laid. Marvelous as has been the progress of medicine during the last century—unrivalled in any period of the world's history—yet it would have been impossible had we not been taught by Hippocrates the value of observation and by Harvey the necessity of experimentation; even from the Galenic era, although we may well avoid its mistake of blind adherence to accepted doctrines, we may learn, to our advantage, a due respect for the achievements of our predecessors.

CEANOTHUS AMERICANUS L
AS A HEMOSTATIC
A RÉSUMÉ OF RECENT INVESTIGATIONS
INTO THE
CHEMISTRY, PHARMACOLOGY AND CLINICAL USE OF THE DRUG

By

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Ceanothus Americanus

Pharmaceutical history is replete with discoveries, both accidental and intentional, of valuable plant principles. The isolation of these active constituents has generally followed the empirical use of the drug.

Recent investigation of the plant Ceanothus americanus has disclosed an alkaloidal principle possessing coagulative action which justifies its use as a hemostatic. Literature records the use of the drug as a "styptic for restraining hemorrhage from wounds" [1] as early as 1836, but no further mention was found of its use in the control of bleeding until 1879 when it was described as a remedy in passive

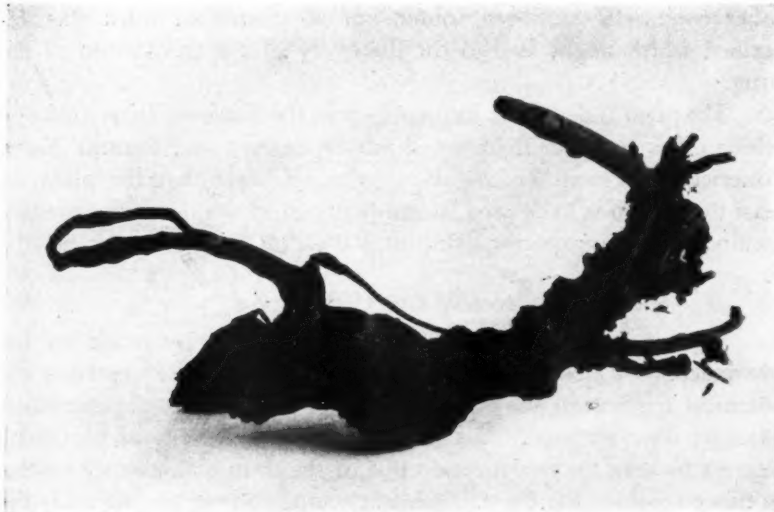

ILLUSTRATION NO. 1
Typical old root of Ceanothus americanus.

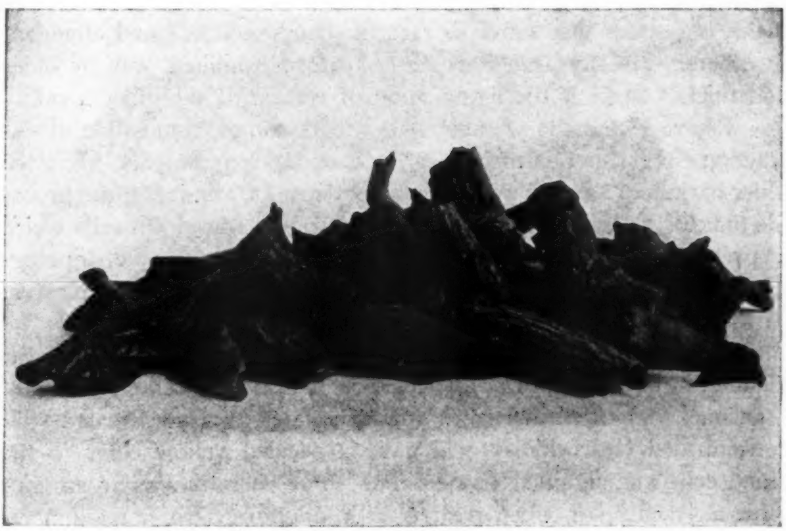

ILLUSTRATION NO. 2
Typical root bark of Ceanothus americanus.

uterine hemorrhage.[2] Reference to the use of the drug in many other conditions has been found, but no controlled work was described which might lead to the discovery of the true action of the drug.

The plant is described incompletely in the *National Dispensatory*,[3] which gives the habitat of the shrub as Eastern and Central North America. My own investigation would indicate that the plant, at least that which is to be used for medicinal purposes, is more definitely confined to certain specific localities in the Blue Ridge Mountains.

Botany and Histology

Wirth [4] has recently published a comprehensive work on the pharmacognosy of Ceanothus americanus, in which he describes the botanical features of the plant, and dwells at length on the characteristics of the root bark. His work on the root bark is of particular interest because the therapeutic value of the drug undoubtedly resides in this portion of the plant. It is interesting to note that he finds the root bark much thicker than the stem bark, averaging one-eighth the diameter of the root. He mentions a reddish brown substance frequently found in the outer portion of the cortex. This substance is undoubtedly the "resin" mentioned by both Groot [5] and Clark.[6] He found rosettes and occasionally prisms of calcium oxalate in all specimens, but states that starch is rare in some specimens and abundant in others. He says "an interesting feature exhibited only by older and thicker barks is the lignification of certain of the phloem cells."

I have found the younger barks to be almost impossible of extraction either for pharmaceutical or chemical experiments, while the older barks can be used with satisfactory results, and it is quite probable that this difference is due to the lignification of phloem cells which is present in the older barks. Two excellent microscopic drawings (by Wirth) are reproduced here to illustrate this greater lignification of the older barks.

Experiments conducted by Wirth to show the presence of the alkaloid in the root bark are not entirely conclusive but he found that "specimens softened in slightly alkaline water and then treated with concentrated hydrochloric acid gave a decided yellow color to the stone cells and lignified tissue. The stone cells of similar sections gave a green color when treated with sulphuric acid potassium dichromate mixture, both reactions taking place within a very few minutes." It is significant that both of these reactions were obtained by

Clark in experiments with the alkaloid. Wirth obtained crystals in one case at least by soaking dry bark in alcoholic picric acid, which he says, "may have been those of an alkaloidal picrate."

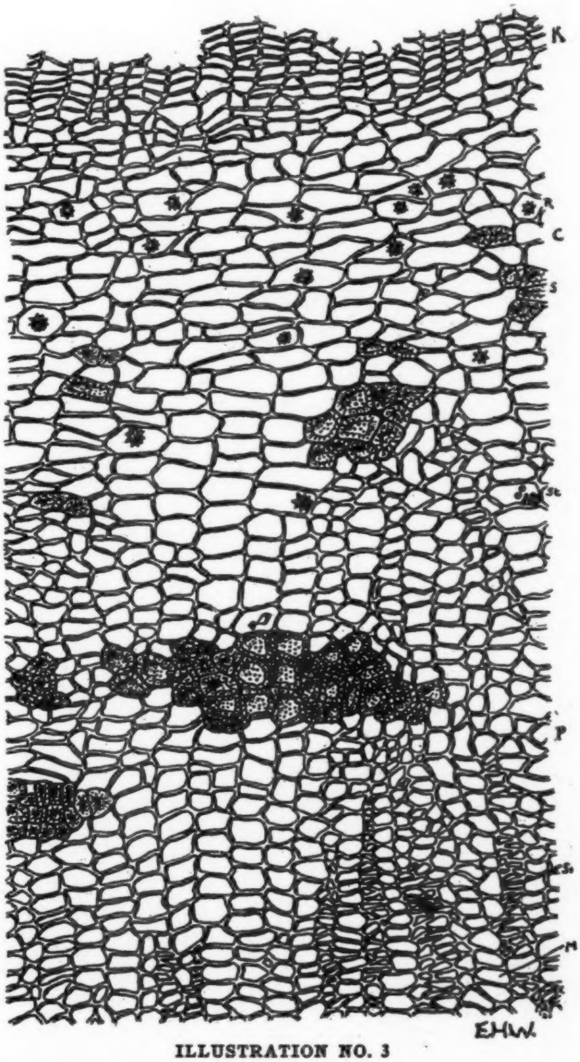

ILLUSTRATION NO. 3

Transverse section of the young root bark of Ceanothus americanus. Wirth, E. H.: The Pharmacognosy of Ceanothus Americanus. Am. Journ. Pharm., Vol. 98, No. 10, p. 511, October, 1926.
K—cork, C—cortex, P—phloem, S—stone cells, Si—sieve, R—rosettes of calcium oxalate, St—starch, and M—medullary rays.

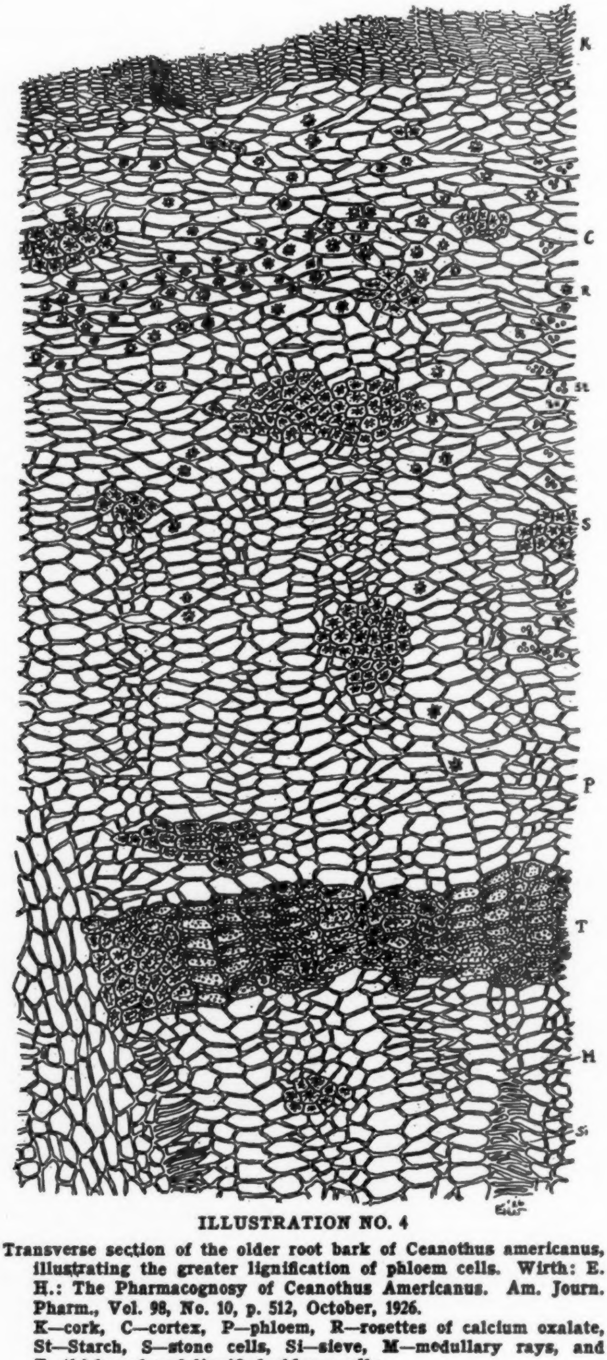

ILLUSTRATION NO. 4

Transverse section of the older root bark of Ceanothus americanus, illustrating the greater lignification of phloem cells. Wirth: E. H.: The Pharmacognosy of Ceanothus Americanus. Am. Journ. Pharm., Vol. 98, No. 10, p. 512, October, 1926.

K—cork, C—cortex, P—phloem, R—rosettes of calcium oxalate, St—Starch, S—stone cells, Si—sieve, M—medullary rays, and T—thickened and lignified phloem cells.

Chemistry

My investigation into the chemistry of the plant was begun early in 1925. The general method given in the U. S. P. IX for alkaloid analysis was followed, but results were disappointing, and it was not until various organic solvents were employed that encouraging results were obtained.

By extracting the ground drug with chloroform and evaporating the solvent, a residue was procured which was similar in appearance to a yellow scale salt. This residue, obtained in numerous extractions, had a peculiar pungent odor and a very characteristic yellowish color. It gave alkaloidal reaction with Mayer's test but appeared to be highly impure.

Reference had been found in the literature to the presence of an alkaloid, or mixture of alkaloids, of which Gordin [7] says he obtained 0.2 per cent.

Clark [6] continued the investigation into the chemical constituents of the drug, and isolated a complex mixture of alkaloids distinctly granular in character and melting at approximately 190 degrees C. He also obtained a crystalline alkaloid which was perfectly white and seemingly very pure. Clark has obtained another substance having a melting point of about 125 degrees C., which he termed " 'resin' for lack of a better name." He obtained alkaloidal reactions with most of the common reagents both from solutions of the amorphous mixture and the crystalline alkaloid.

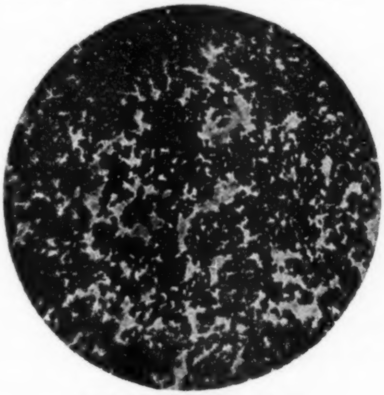

ILLUSTRATION NO. 5
Crystalline Alkaloid extracted from Ceanothus americanus. Clark, A. H.: The Alkaloids of Ceanothus americanus. Am. Journ. Pharm., Vol. 98, No. 3, p. 149, March, 1926.

ILLUSTRATION NO. 6
The Amorphous Alkaloids of Ceanothus americanus. Clark, A. H.: The Alkaloids of Ceanothus americanus. Am. Journ. Pharm., Vol. 98, No. 3, p. 149, March, 1926.

Alkaloidal assay of the drug is made particularly difficult by the presence of a red color, which Gerlach [8] has called ceanothus red. I have been able to free the drug from the color and greatly facilitate the isolation of alkaloid, by extraction with water made slightly alkaline with ammonia. Making use of this preliminary extraction it has not been difficult to extract 0.3 to 0.35 per cent. of the amorphous alkaloid with a melting point between 185 degrees and 190 degrees C.

The alkaloid exhibits certain peculiar characteristics regarding the solubilities and the formation of salts, most of which are mentioned in Clark's recent work. It is freely soluble in acetic acid. It is readily soluble in methyl, ethyl, and butyl alcohols, less so in chloroform, and slowly soluble in sulphuric ether. Ethyl acetate is also a good solvent for the alkaloid, but is not suitable for extraction processes because it readily dissolves much other organic matter present in the drug.

A great deal of my work has been done on extracts of the drug to establish satisfactory qualitative tests to show the presence of the alkaloids in Ceanothyn.* Reliable results are obtained by following the technic given below, and indicate their uniform presence.

> Boil 25 cc. Ceanothyn to remove alcohol, reducing the bulk to 15 cc. Dilute with 25 cc. Water. Make distinctly alkaline with Potassium Hydroxide. Shake out with three portions chloroform—25, 15 and 10 cc. Combine chloroform washings and filter. Evaporate chloroform on water bath to recover alkaloid extracted. Test from acid sol. with Mayer's reagent.

Pharmacology

Groot [5] instigated the first investigation into the pharmacology of the drug. He used Ceanothyn and the amorphous alkaloids described by Clark.

It was believed at this time that the drug was probably an hemostatic of the constrictor type, but Groot's first experiments on dogs disproved this theory. He says, "one of the most striking observations in this preliminary work was that, instead of the anticipated rise in blood pressure, when either the alkaloids or the hydroalcoholic preparation were injected intravenously, there was always a marked depression in the blood pressure records as recorded

* Ceanothyn is an extract of the drug Ceanothus americanus, marketed by Flint, Eaton & Co., Decatur, Illinois. It is chemically and physiologically tested for the uniform presence of the alkaloids.

kimeographically by mercury manometer in mammalian experiments on dogs." He also says, "that for the dosage used, at least, and for one which produced an almost maximum fall of blood pressure, there was no apparent effect on the heart." I have reproduced here, without data, two kimeographic tracings from Groot's work merely to illustrate what has been said regarding the hemodynamic effect produced in dogs by intravenous injections of the drug extract and the alkaloids.

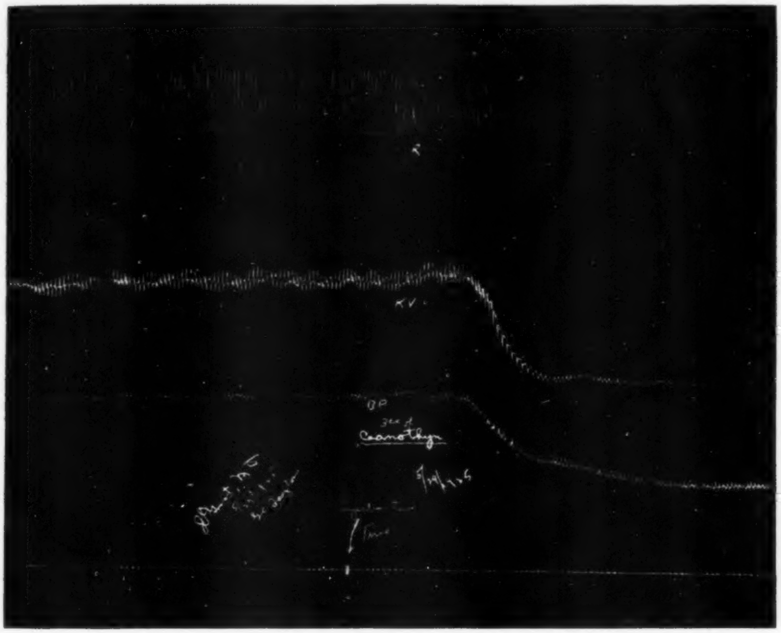

ILLUSTRATION NO. 7

Kimeographic tracing illustrating the effect produced on the blood pressure in dogs, by an intravenous injection of 3 cc. of Ceanothyn. Groot, Jas. T.: The Pharmacology of Ceanothus americanus. The Journ. of Pharm. and Exper. Therap., Vol. XXX, No. 4, p. 279, February, 1927.

These early experiments eliminated the theory of constrictor action which had been advanced and caused Groot to begin a series of tests to determine the possible effects on coagulation time. Marked depressions in the coagulation time of dogs' blood were noted following intravenous injections of the drug extract, or the alkaloids, and a series of carefully controlled experiments was planned using

an oral administration of the drug extract to human subjects. In these preliminary coagulation experiments, depressions in coagulation time of twenty-five to fifty per cent. were common. Comparative tests were arranged wherein a control solution was administered under identical conditions. These tests made with the control solution proved that the coagulative action produced by administration of the marketed preparation was not due to the menstruum or vehicle used in its manufacture.

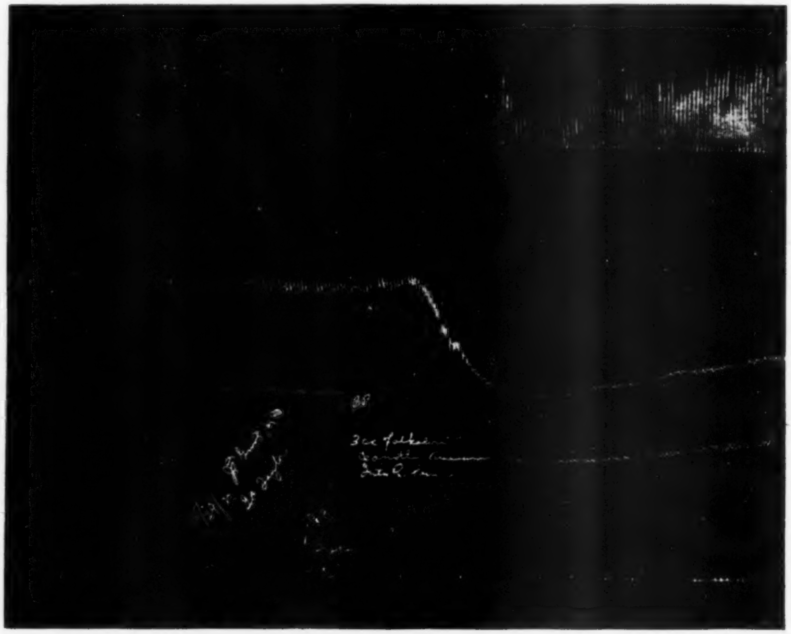

ILLUSTRATION NO. 8

Kimeographic tracing illustrating the effect produced on the blood pressure in dogs, by an intravenous injection of 3 cc. of a 1 per cent. Sol. of the amorphous alkaloids. Groot, Jas. T.: The Pharmacology of Ceanothus americanus. The Journ. of Pharm. and Exper. Therap., Vol. XXX, No. 4, p. 276, February, 1927.

Groot undertook an experiment to show graphically the actual occurrence of coagulation events, plotting the coagulation time of the subject every five minutes following the oral administration of a half ounce dose of Ceanothyn. He used the capillary tube method for determining the coagulation time as described in his recent published work. This graph is copied below and in Groot's words shows

"the regularity of the depression, its full extent and maintenance time. It takes about fifteen minutes for the first appreciable effect to manifest itself. This effect gradually increases to its approximate maximum twenty minutes after administration and is maintained for about fifty minutes longer, and gradually wears off after that time. The total elapsed time from the moment any depression is noted before the normal coagulation time is re-established is eighty-five minutes."

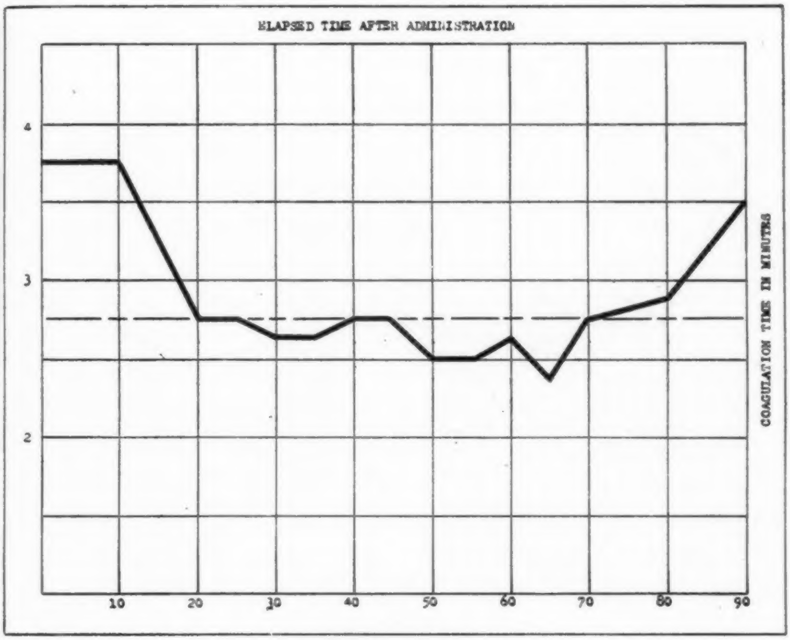

ILLUSTRATION NO. 9

Detail graph of coagulation events. Groot, Jas. T.: The Pharmacology of Ceanothus americanus. The Journ. of Pharm. and Exper. Therap., Vol. XXX, No. 4, p. 285, February, 1927.

All of the experimental work indicates that the clotting time is shortened (within limits) in direct proportion to the amount of Ceanothyn administered, and that the occurrence of coagulation events would follow closely the detailed curve shown above.

Groot cites three groups of cases in which this observation has been almost mathematical in uniformity. In one group of thirteen cases he administered orally, 12 cc. doses of Ceanothyn, and obtained

an average reduction of 41.8 per cent. in coagulation. A second group (seventeen cases) in which he administered 8 cc. doses, the average reduction was 32.8 per cent. In fourteen cases where he gave 10 mg. doses of the purified mixed alkaloids in capsule, he obtained an average depression in coagulation time of 25.8 per cent.

All of these cases are reported as pathologic and were closely observed for any signs of untoward effect. Regarding this observation, Groot concludes that an "oral administration of the hydroalcoholic extract of Ceanothus americanus has apparently no untoward effects on human patients as judged by the absence of nausea, vomiting, epigastric pain, headache and syncope."

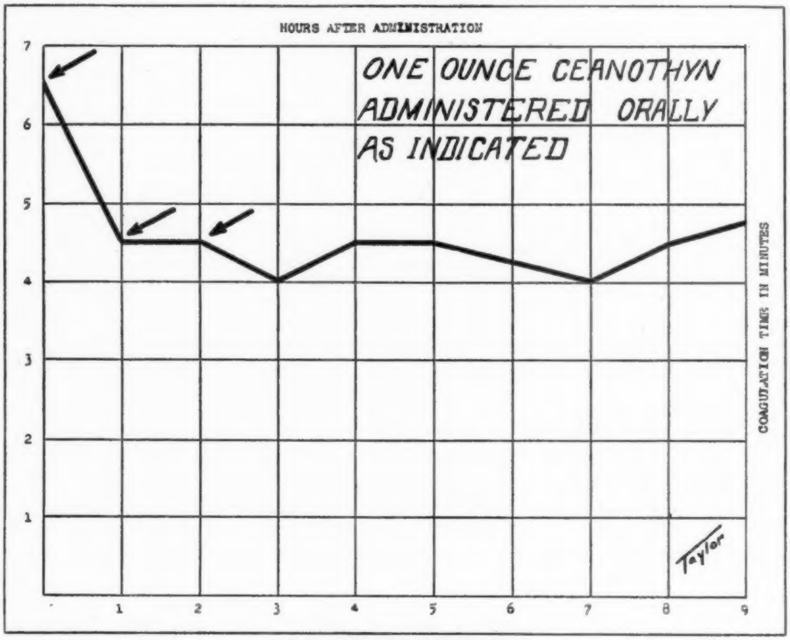

ILLUSTRATION NO. 10

Illustrating the depression in coagulation time affected by the administration of three one-ounce doses of Ceanothyn at hourly intervals.

I have observed many phases of the effect on coagulation time produced by large and repeated doses of Ceanothyn orally administered to both animal and human subjects. Most of these experiments were conducted to determine the safety with which the drug could be administered. One typical experiment illustrates the effect on coagulation time following the oral administration of three ounces

of the preparation within two hours. The test was made on a normal male subject and no untoward symptoms could be detected.

This and many other experiments indicate that on human subjects the maximum effect on coagulation time can be obtained from single one-ounce doses, but that repeated dosage is necessary to sustain a depressed coagulation time over a period of hours. It is the opinion of both Groot and Payne, that single large doses of Ceanothyn depressed the coagulation time quite rapidly, but that the effect is not long sustained. Groot cites a return to normal after ninety minutes following the administration of a single one-half ounce dose.

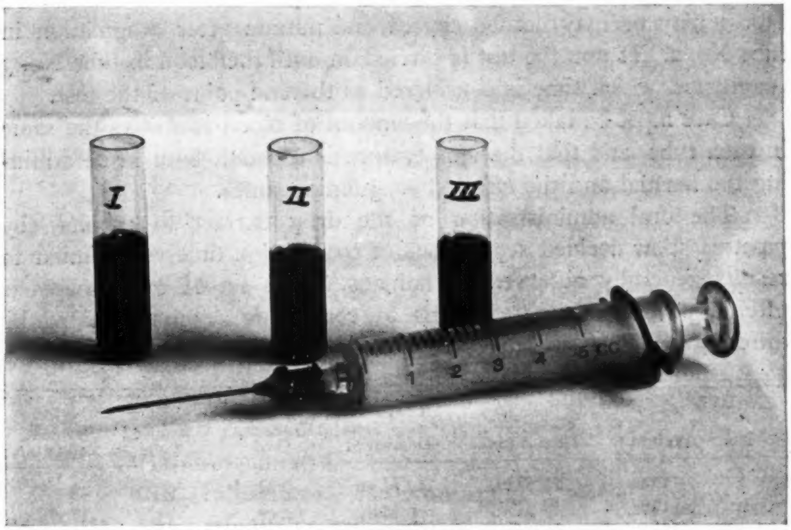

ILLUSTRATION NO. 11
Tubes used for determining the coagulation time.

In most of my work on human subjects I have used the capillary tube method of determining the coagulation time as described by Payne.[9] For comparative results I have recently completed a series of experiments on rabbits adapting the method of Howell [10] to animal work. In this set of animal experiments I have withdrawn the blood directly from the heart, veno-puncture being impractical for the amount of blood required. In Howell's method it is essential that the blood be withdrawn with minimum contamination by thromboplastin from the tissues. Coagulation then depends primarily on the thromboplastin released by the destruction of blood

platelets and is, of course, much longer delayed, presenting a better opportunity for the observation of differences in the clotting time. The greater amount of blood used also influences the time required for coagulation. After the blood has been withdrawn it is divided equally in two or more sterile glass tubes of uniform size, and allowed to remain at rest for several minutes. To determine the end point tube No. 1 is then carefully tilted at one minute intervals until the blood in the tube is jelled (the tube may be inverted without spilling). The blood in tube No. 2, not having been agitated, is still fluid at this time and the test is carried on by tilting this tube once each minute until coagulation takes place. The blood in tube No. 3 may or may not be clotted one minute after coagulation in tube No. 2. If not, the test is carried on until the blood in tube No. 3 coagulates, which time is considered as the end point of the test.

Care must be taken that the amount of blood is always the same in each tube, and that the temperature is constant both in determining the normal and the effected coagulation times.

The oral administration of the drug extract to rabbits (by pipette) show decided depressions of coagulation time very similar to results generally observed on humans. This set of experiments is offered particularly as a means of comparing results obtained by different methods of determining the coagulation time.

No.	Weight	Coagulation Time Normal	Coagulation Time Depressed	Dose Ceanothyn Oral	Elapsed Time	Per cent. Reduction
1	70 Ozs.	23 Min.	13 Min.	2 cc.	90″	43.48
2	64 Ozs.	17 Min.	9 Min.	2 cc.	75″	47.06
3	68 Ozs.	21 Min.	11 Min.	2 cc.	105″	47.62
4	68 Ozs.	17 Min.	12 Min.	2 cc.	150″	29.40
5	65 Ozs.	15 Min.	8 Min.	2 cc.	90″	46.80
6	82 Ozs.	17 Min.	7 Min.	2 cc.	75″	58.80
7	82 Ozs.	16 Min.	10 Min.	2 cc.	60″	39.37
8	70 Ozs.	15 Min.	8 Min.	2 cc.	105″	46.66
9	68 Ozs.	16 Min.	11 Min.	2 cc.	105″	31.25

Considering the body weight of the animal, dosage is comparatively large in these experiments. Although it is impractical to draw conclusions from such a few tests, there is an apparent relation between the elapsed time after administration, and the amount of reduction in clotting time which corresponds very closely to results observed on human subjects.

The animals were carefully observed for any signs of discomfort or distress occasioned by the administration of such large (comparatively) doses of Ceanothyn, but no untoward symptoms could be detected.

Resin

The substance which has been called "resin" has not been thoroughly investigated and its true nature has not been established. In experiments which I have made following the oral administration of this substance to normal subjects I have been unable to draw any conclusions as to a positive effect on coagulation time. In a few cases there was an apparent depression but in other cases there was no appreciable effect. Even in those cases where a positive reaction seemed apparent the effect was so irregular as to make the results valueless. It seems that any depression which has been obtained from the administration of the resinous substance can be attributed to physical or chemical combination with the alkaloid.

Blood Reactions

Tharaldsen [11] in his work at Northwestern University observed the effect of an oral administration of Ceanothyn upon the coagulation time of forty normal persons. He obtained an average depression of 41 per cent. within forty-five minutes after the administration of single half-ounce doses. He used the method of Peterson and Mills [12] for determining the coagulation time, obtaining the blood by veno-puncture in the arm. This confirmation of Groot's work on coagulation was preliminary to his recent experiments, conducted on dogs, guinea pigs, chickens, and humans, which were devised to test the effect of the alkaloids on the concentration and activation of the various factors entering into the coagulation process.

Regarding possible changes in the chemical constituents of blood, Tharaldsen shows a series of analyses on whole blood and blood plasma both before and after the administration of the alkaloids. He notes some changes in the concentration of the blood constituents, but thinks they are not sufficiently great to represent a deviation from the normal variance of these concentrations in human blood.

In his study of the effects on coagulation mechanism, Tharaldsen followed Howell's [13] theory that circulating blood contains all

necessary clotting factors, fibrinogen, prothrombin and calcium, but that these are prevented from reacting in the blood stream by the presence of antithrombin, which holds the prothrombin in combination. In shed blood the restraining effect of antithrombin is neutralized by the action of thromboplastin (tissue extract) derived both from the blood element and from the tissues.

He devised a series of experiments to determine the effect of the alkaloids on these individual factors of coagulation. In these tests he determined that soluble fibrinogen was not changed to insoluble fibrin, nor was the action of calcium in the conversion of prothrombin to thrombin, accelerated or replaced.

Using hen's blood which he says does not contain thromboplastin, except by contact with broken tissue, he endeavored to determine whether or not the neutralizing action of antithrombin on prothrombin was effected, and draws the conclusion that such is not the case. He found, however, that the action of thromboplastin in the neutralization of antithrombin was accelerated. This acceleration of thromboplastin was observed also when similar experiments were conducted on peptonized dog's plasma, which is analogous to hen's blood.

Tharaldsen says, "the natural conclusion to be drawn from all the evidence is therefore to look upon the alkaloid as an accelerator of the action of thromboplastin, probably acting catalytically in the combination of antithrombin and thromboplastin."

He concludes that the oral administration of the alkaloids cannot induce intravenous clotting because they do not perform the functions of thromboplastin nor bring about the release of thromboplastin from the blood or tissue elements, although they do function in relation to thromboplastin.

Tharaldsen's theory of the effect produced on the coagulation mechanism, by the oral administration of Ceanothyn, may be graphically illustrated by the use of lines and arrows to indicate the acceleration of the action of thromboplastin.

The formation of the clot then would take place in a series of steps occurring perhaps simultaneously.

(1) Release of thromboplastin by the destruction of tissue or blood platelets.

(2) Neutralization of the restraining power of antithrombin by thromboplastin to release prothrombin. This action is facilitated and accelerated in the presence of the alkaloids.

(3) Prothrombin combines with calcium to form thrombin. This action is accelerated because of the greater rapidity with which prothrombin is being released as the reaction between antithrombin and thromboplastin is accelerated.

(4) The thrombin combines with fibrinogen to form insoluble fibrin.

(5) Insoluble fibrin enmeshes the blood corpuscles to form the clot.

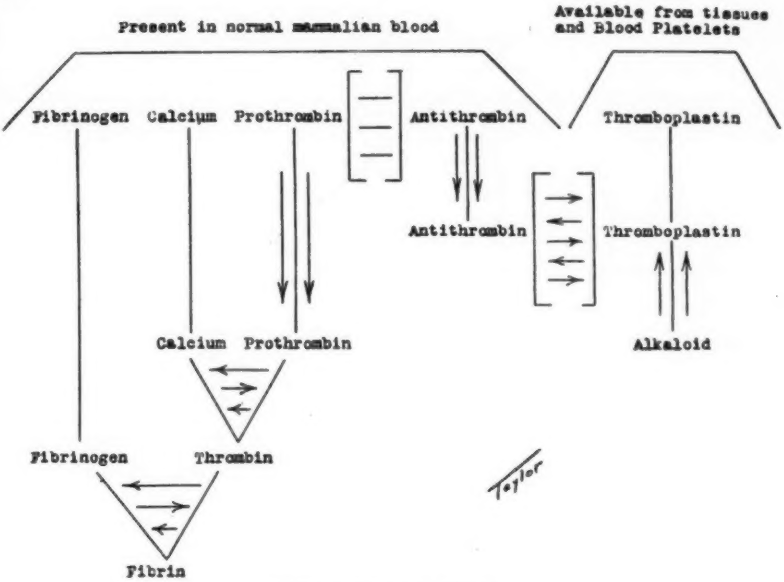

ILLUSTRATION NO. 12

Lines would indicate the normal bonds between the reacting substances. Arrows indicate the accelerated action in the presence of the alkaloids.

Tharaldsen's conclusions that the "alkaloids, orally administered, will not induce intravenous clotting" and that they do "accelerate the action of thromboplastin" would indicate that an advantageous use could be made of the alkaloids by administering them orally in conjunction with tissue extracts containing thromboplastin, especially in cases where there is apparently a paucity of this reacting substance.

Clinical Investigation

Numerous hospitals have made observations on the use of the drug in this actual control of hemorrhage with results which substantiate the experimental work described. One hospital reports

an average depression in coagulation time of 23 per cent. in forty-three cases, twenty minutes after oral administration of single one-ounce doses. This work agrees quite closely with the results shown by Groot in his published work.

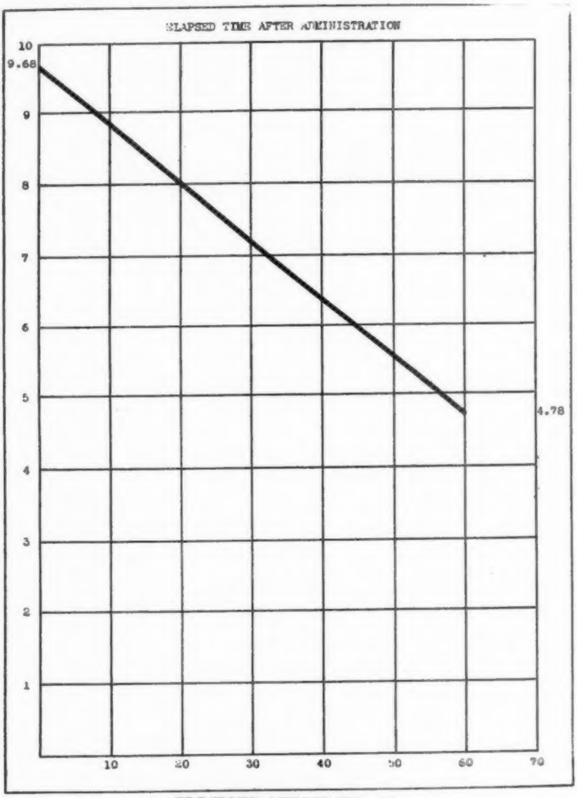

ILLUSTRATION NO. 13

Graphic illustration of the effect on coagulation time produced by the administration of Ceanothyn in eight pathologic cases. Payne, R. J.: The Alkaloids of Ceanothus americanus and their use in control of hemorrhage in Laryngology. Annals of Otology, Rhinology and Laryngology, Vol. XXXV, No. 3, p. 789, September, 1926.

Probably the most interesting clinical work reported to date is that of Payne,[9] who describes results obtained in 234 cases in which he administered Ceanothyn preoperatively. In 225 cases he observed an average reduction in coagulation time of 21.9 per cent., but calls attention to the fact that the normal clotting time in these patients was low. He says "coagulation time is depressed more rapidly and

to a greater extent in those cases in which the normal clotting time is high. Eight pathological cases in which the average normal coagulation time was 9.68 minutes showed an average reduction in clotting time of 50.6 per cent. within one hour following the administration of the solution." The chart given below is copied from his work and shows graphically the result I have noted here.

Payne has grouped his results according to the age and sex of the subjects observed, but concludes that "the effect on coagulation time is not influenced by the age or sex of the patient." His work also agrees with the work of others regarding the rapidity of action and the interval of elapsed time after administration required to produce the maximum effect, which he considers to be approximately forty-five minutes following the administration of one-half ounce doses of Ceanothyn.

Summary

The salient facts regarding the drug Ceanothus americanus and its uses are assembled here. Quotations have been used freely from the work of recent investigators in my effort to explain the type of work which has been done and the conclusions drawn.

It has been shown that the drug contains a mixture of alkaloids which reside in the root bark; that an extract containing these alkaloids has the property of hastening blood coagulation when orally administered; that this effect on blood coagulation is apparent regardless of the age or sex of the subject; that this effect is due to an acceleration of the action of thromboplastin; that the effect is rapid in its onset and is sustained from one to two hours and that no untoward effect has ever been observed following the oral administration of the drug.

To Professor A. H. Clark, Professor E. H. Wirth, and Dr. James T. Groot, of the University of Illinois, School of Pharmacy; to Dr. C. E. Tharaldsen, Northwestern University, and to Dr. R. J. Payne, Washington University, the writer makes grateful acknowledgment for advice and assistance throughout the entire investigation of this drug.

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SAND—FROM MOUNTAIN TO SEASHORE*

By Edward J. Hughes, P. D.†

Assistant Professor of Chemistry

IT SOMETIMES happens that the common things of everyday life are those about which we know very little, and it would be difficult to select a more common substance than the one that we are to consider briefly this evening. Every one is at least familiar with sand, comparatively few have taken the time to reflect upon its origin, its history and its many applications to human progress.

Edward J. Hughes, P. D.

To begin with, sand is not always a pure substance, nor is it considered to have a definite composition. For example, the sand from Bermuda is chiefly composed of carbonate of calcium, while the monazite sand of India, Brazil and the Carolinas contains compounds of the rare earths. But the ordinary sand with which we are concerned is that which now covers hundreds of thousands of square miles of the earth's surface and which is chiefly composed of silicon dioxide, or silica, in the form of broken grains of crystalline quartz.

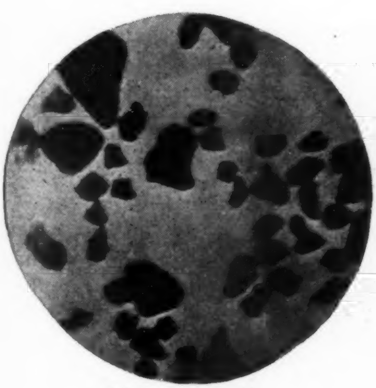
*One of a Series of Popular Science Lectures given at the Philadelphia College of Pharmacy and Science, 1926-27 Season.

†Now associated with Eli Lilly & Co., Indianapolis, Ind.

Sand is produced by the crumbling of the outer surface of the earth's crust, which has been going on for countless ages. As the original or primary rocks have been exposed they have undergone chemical and mechanical disintegration. Even today the stalwart

Beach Sand x 80, Atlantic City.
(Note Rounded Outline.)

River Sand x 80.
(Note Partly Rounded Edges)



Sahara Sand x 10.
(Note Jagged Edges)

Whistling Sand x 25.
From Coast of Wales.

rocks of mountain ranges, such as granite and feldspar, are being laid bare by weathering agencies only to be attacked by water, carbonic acid, quick changes of temperature, frost and lightning. This treatment tends to split and to disintegrate the rocks, reducing them to fine

particles. The powdered material is washed away as clay or mud, while the quartz, which is more resistant and does not undergo further chemical disintegration, remains in the form of broken fragments and becomes sand. A considerable amount of this sand finds its way into the soil, but a very great portion of it is carried by streams into rivers and subsequently into the sea. In desert regions where the broken-down particles cannot be washed away they are blown by the wind, with the result that the grains of sand become well worn and rounded. It is obvious then that Nature's chief transporting and sorting agents for sand are wind and moving water. So thorough is this sorting process that known deposits of sand have been found which contain up to 99.9 per cent. of silica.

In deserts and other dry inland regions where loose sand is exposed to the wind the sand accumulates in hillocks and these are known as sand-dunes. These dunes are moved about by the wind and they form the rolling hills of the desert. In some respects the shifting sand-dunes of the desert are comparable to the waves of the sea. They give serious trouble when they invade fertile and inhabited country, and there are places along the shores of Lake Michigan where they have actually buried swamps, forests and even low hills. In some localities efforts are being made to check their progress, as in the southwest, where railroad companies are temporarily fixing the dunes by spraying them with crude oil. In this connection it is interesting to note that the city of Amsterdam in Holland derives its water supply from sand-dunes that have been erected by wind and wave action along the Netherland coast. This particular section is composed of rather loose sand, in which the city water department plants tufts of reed grass in order to keep the sand from shifting.

SAND AND SOIL

Life is sustained on the earth by the mantle of fertile soil which has also resulted from countless ages of rock disintegration together with the decay of animal and vegetable matter. Sand is an essential factor in good soil, since it tends to keep the soil loose and open. It adds very little, if anything, however, to the nutritive value of the soil. This will be seen from the fact that while silica constitutes more than half of the mineral matter of the soil, yet plants yield from 2 to 10 per cent. of ash when they are burned, of which only about one-twentieth is silica. Some people have the impression that sandy soils are more healthful than those deficient in sand, but more compact soils are warmer than those containing excessive amount of sand.

There is a considerable amount of air in sand, and air is a poor conductor of heat, therefore the heat does not penetrate deeply into the sandy soil where it could later be slowly given up.

Imagine, if you can, the vast ages of time that were involved in the formation of a piece of sandstone such as is used in the construction of a building. Sandstone is made up of grains of sand which have become compacted together by a cementing material and by the weight of other sediments above them. The original sand grains have been worn off the surface of some older rock such as granite as a result of long ages of weathering. They have then been carried away by streams and laid down in deposits along the streams or upon the sea floor and are covered by later formations. The cementing material varies in composition, but is chiefly composed of gelatinous silica, which gradually deposits from solutions upon the sand grains and becomes very hard. The individual grains of such a stone are chiefly composed of quartz, the small particles of this mineral remaining intact because of their hardness and resistance. Large beds of sandstone have been found in New York, New Jersey, Massachusetts, Connecticut, California and Ohio. An immense bed of unusually fine sandstone is being quarried at Berea and Amherst, Ohio. This particular stone has been shown by chemical analyses to contain about 97 per cent. of silica and has been used in the construction of such prominent Philadelphia buildings as Horticultural Hall, the Academy of Fine Arts, University of Pennsylvania and the Academy of Natural Sciences.

Nearly all of the known sources of petroleum oil and natural gas are found in deposits of sedimentary rocks, and chief among these oil-bearing rocks is sandstone. According to the most generally accepted theory, petroleum has originated from animal and plant remains which have become buried in these sandy rocks. The hydrocarbons in petroleum are believed to have evolved and accumulated in the rocks by a process of decay and are held in the deposits of porous sandstone by other layers of impervious rocks or by hydrostatic pressure. California's production of two hundred and thirty million barrels of petroleum oil in 1925 was made possible by deep sand-drilling in the Ventura Avenue section of the Los Angeles basin. Much of this oil was drawn from sandstone at a depth of 5150 feet.

Under the influence of the wind, sand has done much to wear away the rocks and the crags of the earth especially along the seacoast.

WHEN SAND MEETS STONE

There are places along the shore where window glass loses its transparency in a few days. The obelisks in Egypt have been worn away on the sides exposed to the sandy area, and even telegraph poles have been cut down in Southern California by the cutting and gnawing effect of sand-laden winds. Such observations as these have led to an industrial application of sand in what is known as the sandblast. Stone buildings are sometimes cleaned by blowing sand upon them with a powerful blast of air or steam. This procedure is called sandblasting and is also employed in frosting glass and in engraving metals and tombstones. The sandblast furnished one of the earliest methods for redressing the outside of a building. By this means the surface of the stone is removed and a fresh and unstained surface is brought to view. But serious damage may result to many fine buildings through sandblasting operations. This is especially true of buildings faced with limestone. While restoring the surface to its outward appearance of newness, the sandblast cuts away not only the accumulations of dirt and grime but also the outer skin of the limestone that was formed during the process of seasoning. When the pores of this outer surface are removed or opened, Nature's armor against the elements is destroyed and the stone is rendered vulnerable to attack by frost action and the weather. The sandblast would also remove the glazed surface of terra cotta, exposing the porous material beneath to the ravaging effects of weathering.

In a recent bulletin of the United States Geological Survey it has been estimated, as a result of thousands of analyses, that silica constitutes approximately 60 per cent. of the crust of the earth. Of course not all of the silica is there in the form of sand. In fact, much of it is combined with metals in the form of various silicates such as feldspar and mica. It is interesting to note, however, that among the other minerals that have a composition similar to that of ordinary sand are agate, amethyst, onyx, flint, quartz, opal, diatomaceous earth jasper and some others that are not commonly known. Geyserite, a mineral which has deposited from certain spring waters in Yellowstone Park, and silicified wood, from the petrified forests of Arizona, are also chiefly composed of silica. Thus, sand is only one member of a great silica family that constitutes more than half of the outer shell of our planet.

A very interesting form of silica is the diatomaceous earth which is also called infusorial earth and kieselguhr. This fluffy, white substance is used as a packing and polishing powder and also as an absorbent for nitroglycerin in making dynamite. Like sand, it is composed of nearly pure silica and constitutes the remains of multitudes of minute organisms called diatoms and radiolaria. These microscopic organisms extract and secrete silica from sea water just as the shellfishes do calcium carbonate. They live in the upper layers of the water, but after death

THE FLOOR OF THE SEA

An American Sahara from the Air, Death Valley, Cal., U. S. Army Air Service.

their remains sink to the bottom of ponds or of the sea and there form a deposit. It is believed that the greater portion of the floor of the sea is covered by a red mud containing 60 per cent. of sicila, and it is significant that igneous or primary rocks contain silica in about the same proportion.

In considering the immensity of sand deposits one immediately thinks of the great deserts of the earth. It is in these vast white plains of sand that nature seems antagonistic to everything that lives.

It has been computed that the sandy zone traced throughout the breadth of the ancient continents covers an area of about 6,500,000 square miles. And what unspeakable suffering and tragedy have been buried in the silence of the desert. A recent automobile expedition that crossed the Sahara reported traveling for over 300 miles without finding a single drop of water. The sand of the desert becomes unbearably hot during the day and often cools down below the freezing point at night because sand has a low specific heat which prevents it from storing up the heat from the sun's rays. If the soil of the Sahara, for example, contained its normal share of water and were more compact, the heat of the day would penetrate downward and would be given up at night, thereby making the nights warmer and the days cooler than they now are. The nearest approach to the Sahara in America, as regards sand-dunes, heat and aridity, is the East Mesa of the lower Colorado Desert in Southern California. A member of a summer surveying party took a walk in this desert one evening, intending to go around one of the sand hills, and was found two days later hopelessly insane.

On the other hand, there are desert areas in our own country that are being converted into fertile fields by irrigation. In some sections, as for example in the Imperial Valley of Southern California, the reclamation projects have actually succeeded in making the "desert blossom as the rose."

A new desert has recently been discovered in the State of Maine within twenty miles from the city of Portland. Less than a century ago this particular land was a fertile farm section, but the fertile top strata has washed away, exposing a bed of sand, which has since been spreading year by year over the surrounding country. This site is about five miles from the sea and is probably the bed of a long-departed lake.

Nineveh, Babylon and other ancient towns and cities of central Asia are today entombed in sand which has been carried from the desert by the wind, and along the west bank of the Nile are many other towns that are submerged in sand. The discoveries of the future that will throw light upon the history of these ancient peoples of the East are probably hidden at this moment under the sands from Mesopotamian and Arabian deserts.

There are gems of real beauty that are similar to ordinary sand in composition. Among these is the perfectly clear rock crystal which, in addition to its value as a gem, is highly prized in making

fine grade lenses. The purple amethyst belongs in this group and owes its color to the presence of a trace of manganese. The precious opal is essentially composed of silica together with some combined water. In appearance the opal somewhat resembles mother-of-pearl, but shows a brighter play of colors due to the presence of a multitude of little cracks whose angles break up the light reflected off the surface. Such a color is purely physical and would be totally destroyed if the opal were reduced to a fine powder. The agate is another

America's Sahara, The Colorado Desert with San Jacinto Mountain in the Distance. Photo by J. S. Chase.

beautiful form of silica which when cut across shows fine concentric lines and colors which vary to correspond with each successive layer of material.

SAND AND PERPETUAL MOTION

Some very curious facts have been learned with regard to the presence of included gases or liquids, or both, not only in sand but also in other forms of silica such as quartz and amethyst. The sea sand of New Jersey frequently contains microscopic cavities partially filled with

liquid and each containing a tiny bubble of gas. A single grain of sand may show a large number of these cavities if the bubbles are sufficiently small, and they generally show a continuous vibratory motion known as the Brownian movement. In a variety of blue quartz found in Bucks County, Pa., the liquid inclusions contain, in addition to a bubble, minute crystals which are in constant motion, a motion which has been continuous for possibly millions of years. On the other hand, a large pocket of sand was recently discovered in a solid block of marble at Middlebury, Vt. This sand resembles beach sand, and geologists say that the marble was formed under water and the sand was probably caught in the center of the formation.

With enormous quantities of sand at our disposal, one might ask the question, "What is it good for?" But if we consider its importance in the manufacture of glass alone we find that sand justifies itself as one of the earth's greatest endowments toward the progress and the convenience of mankind. From a very remote period to the present day too, white sand has been the chief ingredient in the manufacture of glass. In making glass, a mixture of sand, limestone and soda ash is heated to a high temperature until it forms a clear, syrupy liquid, which solidifies on cooling to form a transparent solid. For a long time Pennsylvania has ranked as the leading State in the production of a glass-sand as well as in the production of quartzite for silica refractories. The most productive area has been in the center of the State, chiefly in Huntingdon, Mifflin and Blair Counties.

Sand is also one of the major constituents in the production of pottery and earthenware. Here the chief functions of sand are to reduce shrinkage and to impart rigidity. The unusually low coefficient of expansion of the silica, especially after firing the mixture, also protects the ware against breakage when exposed to quick changes of temperature.

Enormous quantities of sand go into the production of concrete, which is a form of artificial stone that is largely used in the construction of buildings and highways. Concrete is made by mixing together sand, gravel, Portland cement and water until the mass has the consistency of gruel, then dumping the mixture into wooden forms and allowing it to solidify.

SAND IN PUBLIC HEALTH SERVICE

Sand occupies an important place as a protector of public health in the purification of drinking water, since large quantities of good, even-grained sand are now used in the filtration of municipal water supplies. This process involves more than the simple straining of the water, otherwise disease-producing bacteria might pass through the spaces between the sand grains very easily. But in addition to holding back suspended matter, there is formed on the sand grains a slimy, jelly-like material which serves to entangle and to hold bacteria and minute suspended particles of all kinds. The absence of this gelatinous coating on the sand grains, as for example in sand which has been cleaned, actually lowers the efficiency of the filter-bed. In fact, it has been found that were it not that the filter becomes almost impervious to water it would be better not to remove the dirt and the slime that accumulates.

The relative hardness of sand makes it valuable as an abrasive and it is often used for this purpose in the form of sandpaper and sandstone. In making sandpaper the sharp or rough-edged grains of sand are especially desired. One of the greatest modern applications of sand is in the manufacture of that unusually hard and exceedingly useful artificial abrasive called carborundum. Chemically, carborundum is composed of silicon carbide and about twenty thousand tons of it are now produced annually by the reaction between pure glass sand and finely ground petroleum coke at the high temperature of the electric furnace. Sand constitutes more than half of this furnace mixture, which also contains small amounts of common salt to aid in the fusion and sawdust to render the heated mass somewhat porous.

The fact that sand will form an easily melted substance when strongly heated with limestone gives it an important place in the smelting of certain ores. A substance which reacts with the impurities of an ore to produce a material that can be easily melted and removed is called a flux. If the impurities in the ore are sandy the flux would be chiefly limestone, and if, on the other hand, the impurities are chiefly of a limestone nature the logical flux would be sand. The melted mass that flows away and so concentrates the ore is known as slag.

When pure glass sand is strongly heated by itself in an electric furnace it becomes plastic and cohesive and may be shaped into dishes, flasks and tubing. This material is known as fused silica ware and

is now extensively used in chemical laboratories because of its resistance to most chemicals and to quick changes of temperature. Silica ware may be white and opaque, due to the presence of countless bubbles of air, or it may be transparent as the result of complete fusion. The transparency of this latter variety has been found sufficient to enable one to read a page of printed matter through a block of it ten inches thick.

These few thoughts are sufficient to at least suggest the importance of sand in the natural and the industrial world, for here indeed is an accumulation of the ages, and a boundless store of raw material that is being drawn upon year by year for the increasing needs of man.

MERCURY IN MERCURIC SALICYLATE*

By Ivor Griffith, Ph.M., and Peter P. Ramanuskas, B. Sc.

METHODS for the determination of mercury in mercuric salicylate have often been published and recommended as being preferable to the present U. S. P. method.

One of the outstanding reasons given by most of the analysts is that mercury is lost by volatilization during the digestion in the first stage of the analytical process, thus vitiating the results of the test.

This investigation was undertaken in order:

(a) To determine whether any mercury is lost during the digestion and to ascertain the extent of this loss, if any.

(b) To try a gravimetric method which has been used by this laboratory for years and which for some mercury determinations was known to give uniform and con-consistent results.

Present U. S. P. Method

Assay.—Digest about 0.5 gm. of mercuric salicylate, accurately weighed, in a mixture of 15 cc. of sulphuric acid and 10 cc. of nitric acid contained in a long neck flask in which a small funnel is inserted. Heat it upon a sand bath until the mixture is nearly colorless, then add another 10 cc. of nitric acid, and heat until the mixture is decolorized. Cool the solution, dilute it with 150 cc. of distilled water, add

*A contribution from the Research Laboratory of the Stetson Hospital, Philadelphia.

2 cc. of ferric ammonium sulphate T. S. and titrate with tenth-normal potassium thiocyanate until a permanent yellowish-red color is produced. Each cc. of tenth-normal potassium thiocyanate corresponds to 0.01003 gm. of Hg.

Proposed Methods

Preparation of solution:

In a 250 cc. volumetric flask dissolve about 2.5 gm. of mercuric salicylate, accurately weighed, in 25 cc. of nitric acid.[1]

Insert a small funnel in the flask and heat the contents on a hot plate or sand bath. Add 20 cc. of sulphuric acid, drop by drop, VERY CAUTIOUSLY.

After all the sulphuric acid has been added and the reaction has subsided, bring the contents to a boil and digest until the liquid is nearly colorless, then add cautiously 10 cc. of nitric acid and heat until the liquid is colorless.[2] Cool the solution. Dilute with distilled water and make up to volume at room temperature.

Volumetric Method

Transfer 25 cc. of the prepared solution to a 100 cc. beaker. Add 5 cc. of 10 per cent. nitric acid, 2 cc. of ferric ammonium sulphate T. S. and titrate with tenth-normal potassium thiocyanate until a permanent yellowish-red color is produced.

Each cc. of tenth-normal potassium thiocyanate corresponds to 0.01003 gm. of Hg.

Gravimetric Method

Transfer 25 cc. of the prepared solution to a 300 cc. beaker. Dilute with 75 cc. of distilled water. Add 15 cc. of ammonium hydroxide and 15 cc. of ammonium sulphide solution. Stir and boil gently until the black mercuric sulphide separates readily when the beaker is removed from the source of heat. Then add powdered

[1] Our laboratory custom (chosen for the sake of uniformity in calculations) is to weigh exactly 2.5 gm. of the compound, on a watch-crystal, then transferring it to the flask by washing it in with ether. The latter is then completely volatilized. This is important else trouble will be encountered when the acids are added.

[2] To get rid of the last traces of the yellow oxides of nitrogen, the addition of two or three drops of cold distilled water to the hot acid liquid is very effective, the steam so generated driving off the yellow vapors.

sodium sulphite in small portions until the supernatant liquid is colorless and there is no evidence of free sulphur. Collect the precipitate on a prepared gooch. Wash well with hot water, then once with alcohol and once with ether. Dry thoroughly at 105° C. Cool and weigh.

The weight of mercuric sulphide multiplied by .8622 will give the weight of mercury contained.

Results obtained with a recently purchased sample of mercuric salicylate:

By U. S. P. method.

The results ranged from 57.91% to 62.74% mercury.

By proposed method.

	Volumetric	*Gravimetric*
A	57.46%	57.42%
B	57.68%	57.43%
C	57.42%	57.48%

Conclusions

1. Mercury is not lost during the digestion.[3]

2. The present U. S. P. method yields inconsistent results which are usually high. The reason for this is the difficulty experienced in interpreting the end point in the titration because of the dilution of the solution under examination.

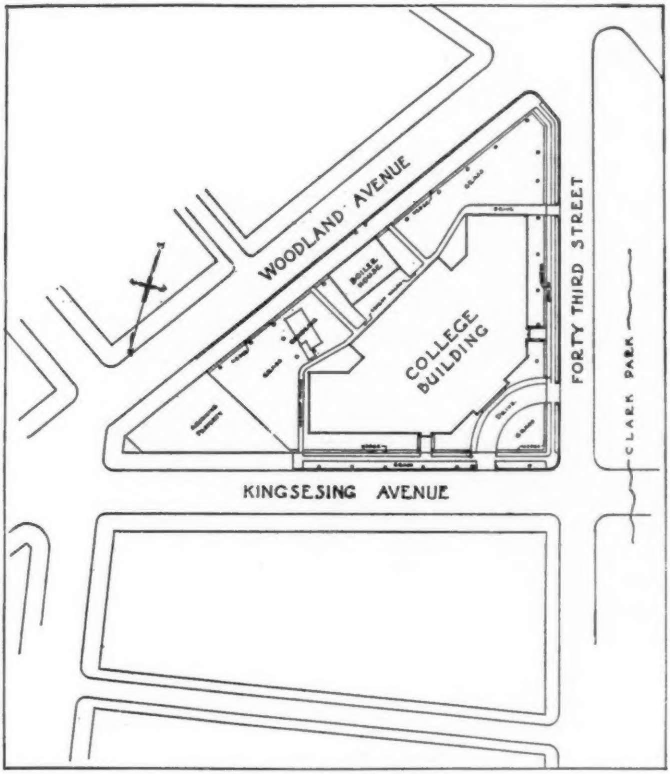
3. The present U. S. P. method with a few modifications may be made to yield very uniform and consistent results.

4. A gravimetric method may be used as an alternative which will give results practically identical with the volumetric method.

[3] An attempt to determine the mercury content of mercurochrome by the same procedure failed through volatilization of mercury, probably as a bromine compound. Obviously, compounds, where mercury is associated with the halogens, do not lend themselves to this particular determination.

THE NEW BUILDINGS OF THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE

THE THOUSANDS of graduates of the Philadelphia College of Pharmacy and Science, resident in every State of the Union, will be pleased to learn that, on March 17, 1927, ground was broken for new buildings at Forty-third Street and Kingsessing Avenue in the presence of hundreds of friends of the institution.

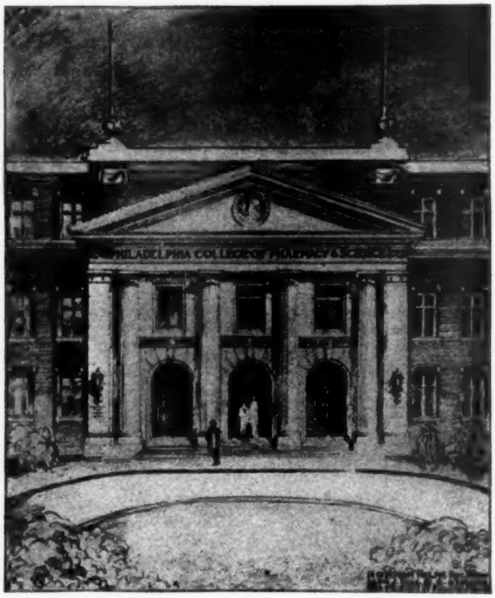


Plan of College Buildings.

The site is a most attractive one of four acres, facing the beautiful Charles H. Clark Park. The buildings, of Georgian-Colonial type, will cover the block of Forty-third Street, Kingsessing Avenue, and Woodland Avenue. The main building will be three stories in height, of reinforced concrete and brick with limestone trim, and a

basement, 141 feet on Forty-third Street and extending 141 feet along Kingsessing Avenue, having two wings of 62 by 141 feet each. The diagonal frontage is 108 feet with a depth to the rear of 135 feet. There will be, also, a building (40 by 60 feet) on Woodland Avenue for heat, light and power, while the college has ground on the north side of Kingsessing Avenue for additional buildings, when needed.

After the invocation by Dr. Horatio C. Wood, a member of the faculty, addresses were made by Admiral William C. Braisted, president of the college and formerly Surgeon General of the United States Navy; Joseph W. England, chairman of the Board of Trustees; Mrs. William E. Lee, of the Women's Organization of the Na-



Front Elevation of New College Buildings.

tional Association of Retail Druggists, and Professor F. X. Moerk, president of the Alumni Association. Professor J. W. Sturmer, Dean of Science, was master of ceremonies.

President Braisted reviewed the history of the college, which started in historic Carpenter's Hall, 320 Chestnut Street, in 1821. He paid a glowing tribute to the memory of Professor Joseph Price

Remington, who, he said, did more to raise the standards of American Pharmacy and build up the institution than any other factor. "This building will be a memorial for those who rendered service in the past," he said, in conclusion, "for the reason, that the College today is erected on a foundation laid by its teachers."

Joseph W. England stated:

> "It is a long cry from 1821 to 1927, and today we are taking a long stride forward in the development of our splendid in-

Ground Breaking Exercises at the Site of the New Philadelphia College of Pharmacy and Science.

> stitution. One hundred years ago the College had quarters in a small building on South Seventh Street, this city, for which a yearly rental of $200 was paid, two professors and perhaps a half-dozen students. Then came the removal of the College to a building of its own on Zane (Filbert) Street in 1832, then to buildings of its own on North Tenth Street in 1868, then the erection of additional buildings in 1892, each change a step forward with many additional students, and now, today, the spade

will turn the ground of this new site, an act that will mark the commencement of the erection of new buildings upon it—buildings having three times the available floor space for teaching purposes the College has on Tenth Street, costing over half a million dollars and accommodating 800 students, and with sufficient ground for additional buildings, when needed.

Mrs. Joseph P. Remington turns over the first spadeful of earth.

"What a contrast betwen the past and present! One hundred years ago the College had rented quarters, two teachers, a handful of students, and a reputation to make. Today the name and fame of our College is known wherever the language of our science and art is spoken, and this rich inheritance comes to us with very definite duties and responsibilities. We must maintain the principles and traditions of the founders. We must serve and sacrifice, also. Let us, therefore, carry-on the work

so splendidly begun and executed, remembering always that while bricks and mortar are essential to a college, it is not bricks and mortar that make a college *great;* it is the brains of earnest, able and devoted teachers reacting with the brains of students, eager to learn, to think and to do, and, most important of all, it is the character of service and end-products of the reaction given to humanity."

Professor Frank X. Moerk gave a most interesting résumé of the work of the Alumni Association of the College in promoting its growth and development since 1864.

A plea for graduates to hold to their profession and not engage in a "lunch counter business under the guise of pharmacy" was made by Mrs. William E. Lee, whose husband was a member of the class of 1872.

Then, in the presence of President Braisted, members of the faculty, board of trustees and hundreds of the alumni and students, the first spadeful of earth was turned up by Mrs. Joseph Price Remington, who used for the purpose a golden spade, decorated with blue and white, the College colors, and on the handle of which appeared the inscription, "Nosse Haec Omnia Salus Est."

Mrs. Remington, as is well known, is the widow of a former member of the faculty for forty-seven years, whose services to the science and art of pharmacy have given him a national and international reputation in the pharmaceutical world.

And with the singing of the College song "Alma Mater" and cheering, the first step in the erection of the new buildings was accomplished, and the exercises were concluded.

OBITUARY

FREDERICK BELDING POWER

IN BRINGING to its close an article of appreciation* of the late Dr. Power's half century of service in the chemical sciences, the present writer chose the following concluding expression as a fitting compliment to the venerable scientist:

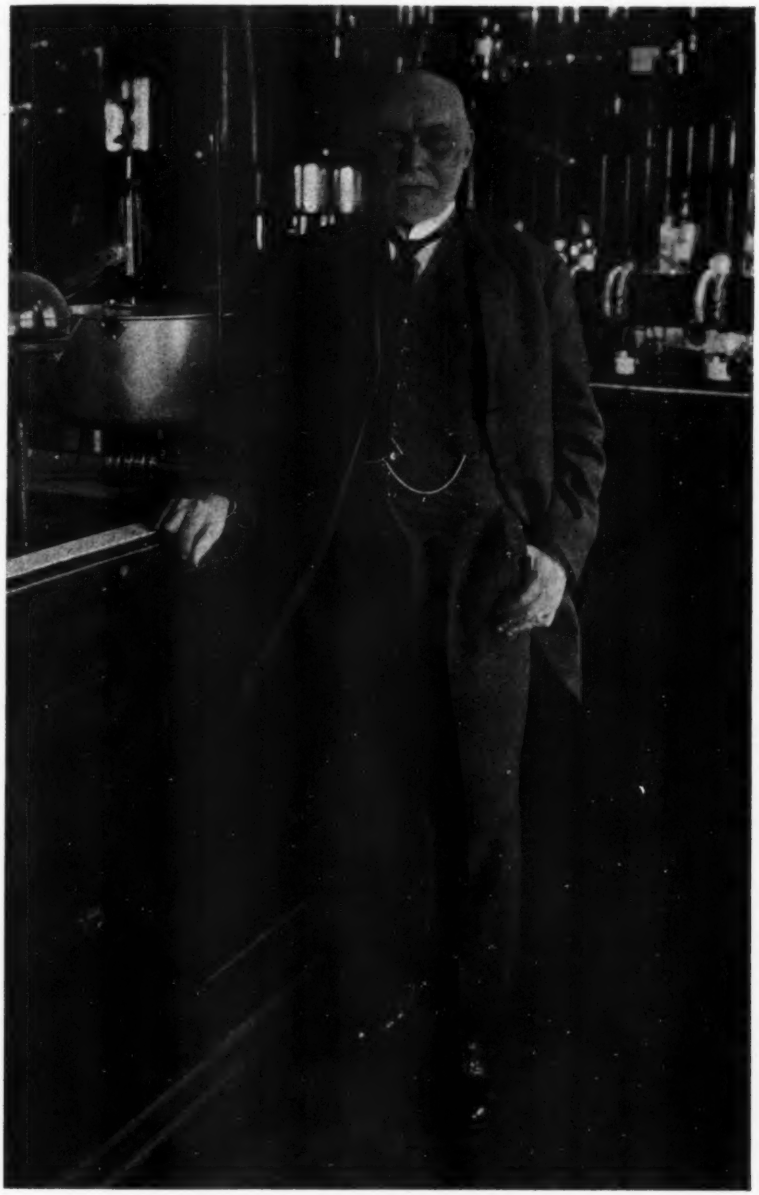
> "Thus endeth the chronicle of a man's achievements over a half century of active, useful service. And the man still carries on into the second half century, serving with equal alertness and mental vigor. Today in scientific Washington no one is more highly regarded than Frederick Belding Power and his laboratory is the shrine of many who come to seek inspiration in the atmosphere of his work-place and in his kindly personality. Said Pasteur: 'Take interest, I implore you, in those sacred dwellings which one designates by the expressive term: LABORATORIES. Demand that they be multiplied, that they be adorned; these are the temples of the future—temples of well-being and of happiness. There it is that humanity grows greater, stronger, better.'
>
> "Truly the laboratory of Frederick Belding Power has fulfilled in every sense Pasteur's immortal sentiment."

But that was yesterday—and today Frederick Belding Power is gone to his eternal reward.

A recent news edition of the *Journal of Industrial and Engineering Chemistry* is quoted in the following paragraph:

> "Frederick Belding Power, who was born in Hudson, N. Y., in 1853, died as a result of heart failure on March 26 at his apartment in Washington, D. C.
>
> "Dr. Power, who was in charge of the Phytochemical Laboratory of the Bureau of Chemistry, Department of Agriculture, which post he had held since 1916, was a graduate of the Philadelphia College of Pharmacy, Class of 1874, and received the degree of Ph.D. from Strasburg in 1880. He was in charge of

*A Half Century of Research in Plant Chemistry. A Chronological Record of the Scientific Contributions of Frederick Belding Power. (*Amer. Journ. of Pharm.*, August, 1924.)



FREDERICK BELDING POWER

the chemical laboratory of the Philadelphia College of Pharmacy from 1880 to 1883, was professor of pharmaceutical chemistry and materia medica at the University of Wisconsin from 1883 to 1892, was director of the laboratories of Fritzsche Brothers from 1892 to 1896, and from 1896 to 1914 was the head of the Wellcome Chemical Research Laboratories in London. Dr. Power was a member of the Committee of Revision of the U. S. Pharmacopeia in 1890, first vice-president of the Pharmacopeial Convention of 1920, and exercised great influence in raising the standards of the pharmacopeias in both the United States and Great Britain. Dr. Power was always identified with phytochemistry and the chemistry of essential and fatty oils, having spent more than fifty years in the work of disentangling complex molecules among botanical products. His work upon the constitution of chaulmoogric acid is a notable example. At the time of his death, Dr. Power was engaged in bringing together the data resulting from his life's work and observations and it is a great loss that this work could not have been completed."

Truly Science has lost an exponent who possessed the unusual gift of linking a rich and a long experience with modern theory and practice, and who permitted his expansive retrospect to affect neither his viewpoint nor vision.

Too often, scientists, long in the work, have not been able to grow with their sciences.

Frederick Belding Power was an exception.

Blessed be his memory.

IVOR GRIFFITH.

SCIENTIFIC AND TECHNICAL ABSTRACTS

Repellents of Blowflies.—Certain species of blowflies—primarily the screw-worm fly and secondarily the green-bottle fly and the black blowfly—cause losses estimated at $4,000,000 or more annually because of their attacks on livestock. They are of particular concern to raisers of cattle, sheep, and goats on the ranges. When the screw-worm flies are abundant they are strongly attracted to the slightest scratch or bloodspot on the skin of an animal. Under favorable conditions they lay eggs in such wounds, and the larvæ hatch and start feeding on the living tissues. If treatment is not administered promptly death of the animal often results.

Ranchmen are using various home remedies, such as axle grease and lamp-black, but probably proprietary "screw-worm killers" of one sort or another are now most prevalently used. These consist largely of crude carbolic acid, which, although it kills the worms with which it comes in contact, is also very poisonous to animals. As a result many animals are killed by the treatment.

In view of this situation the United States Department of Agriculture has for some time been engaged in a study to find a material that will kill the larvæ and prevent reinfestation by repelling the flies. In all, about 350 compounds and mixtures have been tested to determine their repellent or attractant action. The results of this study, as applied to the screw-worm, are reported in Department Bulletin 1472-D, "Chemotropic Tests With the Screw-Worm Fly," just issued and now ready for distribution.

A number of the essential oils are good repellents, among which are Ceylon citronella oil and American pennyroyal oil, commonly used as mosquito repellents. Powdered pyrethrum and derris, both of which are valuable contact insecticides, are effective in repelling screw-worm flies. Of all the materials tested as repellents against the screw-worm fly, however, certain products obtained from the pine are among the best. These include pine oil, crude turpentine, pine tar, and pine-tar oil. In view of the cheapness, availability, nontoxicity, and adhesiveness of pine-tar oil, the investigators are of the opinion that this is the best material among all of those tested to use upon wounds of domestic animals to protect them against the screw-worm fly.

The data presented in the bulletin, which are largely a result of laboratory investigation, serve as a basis for further tests on living animals. Such tests are now under way. Furthermore, it is felt that these studies are a step in the direction of obtaining a better insight into the fundamental principles underlying the responses of insects to various chemical substances.

A copy of the bulletin may be obtained as long as the supply lasts by writing to the United States Department of Agriculture, Washington, D. C.

New Paint Remover from Factory Waste.—An effective paint and varnish remover can now be made by a process discovered by Max Phillips and M. J. Goss, chemists of the Bureau of Chemistry, who have just completed an investigation on the utilization of para cymene, which comes from an oil obtained as a by-product in making paper pulp from wood.

Department chemists in recent years also have worked out processes for utilizing such wastes as straw, rice hulls, peanut hulls, and corncobs, as well as for the more profitable utilization of various cull fruits and vegetables. Several commercial concerns are now making salable commodities from large quantities of cull oranges and lemons by these new processes.

The oil from which the new paint and varnish remover is made was until recently almost wholly an economic waste. It has been variously estimated that from 750,000 to 2,000,000 gallons of this material are annually produced in the sulfite pulp mills of the United States. The paint and varnish remover is prepared by mixing para cymene with grain alcohol, methanol, and acetone, in equal parts by volume.

The most effective method for removing paint and varnish is to apply the new remover to the surface to be treated, and after three to five minutes the softened paint or varnish may be very easily removed by means of a scraper. This remover has been patented by Phillips and Goss and dedicated to the people of the United States.—*Jour. Ind. and Eng. Chem.*, 1927, p. 338.

Chlorpicrin as an Insecticide.—Chlorpicrin or trichloronitromethane has been used in chemical warfare as a moderately toxic, somewhat lachrymatory, "vomiting gas." A. L. Strand (University

of Minnesota, Agric. Extension Div., Special Bulletin No. 102, 1926, 1-19) recommends the use of chlorpicrin as an insecticide for mill and household insects, and describes methods for its use in the fumigation of flour and cereal mills, upholstered furniture, and dwelling houses. The chlorpicrin is mixed with an equal volume of carbon tetrachloride and applied from an atomizing apparatus. The amount of chlorpicrin required per 1000 cubic feet of space is 1.25 pounds for dwellings, two pounds when furniture is treated, and five pounds for milling machinery. The period of exposure to the vapor should be six to twelve hours.—*Jour. Fr. Inst.*, 1927, p. 386.

MEDICAL AND PHARMACEUTICAL NOTES

Hydrogen Peroxide as an Adulterant of Carbonated Beverages.—The March number of "Health," the publication of the New Hampshire State Board of Health, notes that hydrogen peroxide is now being used as a preservative in "chocolate soda." As the commercial forms of this preservative are apt to contain stabilizers, the New Hampshire Board forbade the use in beverages unless free from such, and also directed that the peroxide should be completely decomposed by the time the beverage is shipped and that it shall not be used to correct any lack of cleanliness in manufacture. It appears from recent investigations that the peroxide persists for a long time in beverages prepared by the cold process and such are in violation of the law. Notification is therefore given in the State that beverages containing hydrogen peroxide are forbidden.

H. L.

Paraphenylenediamine in Hair and Toilet Preparations.—Notwithstanding the efforts of sanitarians to prevent the use of this poisonous ingredient in applications for the hair, such use is frequent. With the beginning of the present year the City of New York has established a drastic prohibition of the substance, as well as lead and mercury in any hair-dye or other toilet preparation intended for human use. It is stated that Chicago is also considering the adoption of a similar rule. Regulations in this matter meet with strong oppo-

sition from several sources. Manufacturers, retailers and operators of beauty parlors are all arrayed against regulation. A specious argument, but one which seems to have had much effect, is that the restrictions will deny to womankind the use of means for enhancing personal attractiveness. The annual business of distributing toilet preparations is about two hundred million dollars. It seems that it is proper that a business of this magnitude, in which it is well known that highly poisonous substances are largely employed, should be subject to sanitary regulation, but great difficulties have been found in getting even moderate reform. *H. L.*

Acidophilus and Bulgaricus Preparations Being Studied by United States Chemists.—An investigation of the culture of lactic acid-producing organisms found in interstate commerce, especially those intended for use as medicinal agents, is now under way for the purpose of ridding the market of misbranded, deteriorated, contaminated, or otherwise illegal preparations, according to a statement issued by the officials of the Bureau of Chemistry, United States Department of Agriculture, charged with the enforcement of the Federal food and drugs act. The text of the statement follows:

The Bureau of Chemistry made a survey during the summer of 1926 of Acidophilus and Bulgaricus preparations found in interstate commerce. This survey included the bacteriological examination of cultures in liquid milk, in whey combinations, in tablet form, in powder, and in semi-solid media. One hundred and nine samples representing the product of twenty-four manufacturers were secured from points throughout the United States.

Examination of these preparations showed that a relatively large proportion of them, particularly those in carriers other than milk, contained so few lactic acid-producing organisms or were so seriously contaminated with other bacteria as to be practically worthless.

The Federal food and drugs act makes the manufacture or distributor of medicinal products responsible for marketing them in harmony with its provisions. Manufacturers should assure themselves that the organisms are present in significant amounts in these preparations and that the articles are practically free from contaminating organisms. Statements regarding the therapeutic effects of the preparations should be limited to those that can be fully substantiated by the consensus of present-day medical opinion.

Investigation of this class of products will be continued for the purpose of ridding the market of misbranded, deteriorated, contaminated, or otherwise illegal preparations.

Cultures of lactic acid-producing organisms within the time limit, if any, marked upon the package by the manufacturer, should contain a therapeutically or bacteriologically significant number of viable organisms true to the type claimed and should be practically free from contamination.

CALCIUM IN BLOOD CONTROLLED BY NERVES.—The amount of the blood is apparently regulated by the nervous system, Dr. Alfred F. Hess, of New York, well-known expert on calcium deficiency diseases, told the American Society of Biological Chemists at their recent meeting.

The calcium in the blood is diminished by about a third if certain nerves in the abdomen are cut, he stated, and the supply remains low for many days. But if the spinal cord is cut just the opposite takes place, calcium increases in the blood system from 50 to 75 per cent. In other words, the amount of this important constituent in the blood seems to depend quite directly upon the activity and integrity of the nervous system.—*Science Service.*

POISONS KILL BY ELECTRIC SHOCK.—When Socrates died from a dose of poison hemlock he underwent the same physiological processes that the modern criminal does who passes out in the electric chair, according to a theory advanced by Dr. R. Beutner of the medical school of the University of Louisville.

How poisons actually operate to bring about death is a mystery that has hitherto never been explained satisfactorily.

Dr. Beutner told members of the Federation of American Societies for Experimental Biology at their recent meeting that the deadly effect of certain drugs and poisons like strychnine and atropine is caused by electric charges produced somewhere in the brain and nerves. Dr. Beutner described a new type of galvanic cell with an oily layer as a central conductor, in which he has found that strong poisons will exert marked electrical changes, such as a lowering of electrical voltage. "This, then," he said, "shows that violent poisons actually produce electrical changes in an artificial system which, to some extent, reproduces the conditions in a living organism."

Even very minute amounts of poison diluted millions of times by the blood that carries the agent of death to the brain, exert an overwhelming action on the body. Dilutions of poisons of one part in a million cause a marked effect in the type of galvanic cell that Dr. Beutner has used in his experiments while no non-poisonous substance, he stated, will act in the same way in the galvanic cell under similar conditions.

According to this theory, the scientist explained an animal that dies from the effects of a dose of strychnine has suffered a similar injury in its brain as if it had been struck by lightning or electrocuted. The same conditions hold good for the reactions of strong poisons given for therapeutic purposes. When exceedingly minute doses of strychnine are given as a tonic or morphine is administered to relieve pain, the electrical charges are so moderated in their distribution to the brain and nervous system as to cause a beneficial reaction.—*Science Service.*

NEWS ITEMS AND PERSONAL NOTES

News Items from the Philadelphia College of Pharmacy and Science.—Ground was broken for the new college building on the site at Forty-third Street and Woodland Avenue, Thursday, March 17th, at 2.30 P. M. A short but impressive program was given after which Mrs. Joseph P. Remington turned the first spadeful of ground. Quite a few dignitaries representing the city and other colleges were present. In all it was an inspiring and historic occasion. After an invocation by Dr. Horatio C. Wood, Jr., brief remarks were made by Rear Admiral Wm. C. Braisted, M. D., president of the college; Mr. J. W. England, chairman of the Board of Trustees; Mrs. William Lee, for the W. O. N. A. R. D.; Prof. J. W. Sturmer, Dean of Science; F. X. Moerk, president, Alumni Association.

Athletics.

The Philadelphia College of Pharmacy and Science can be justly proud of its basketball team this year. They have attained great heights in the almost completed season of basketball. The team has a record of thirteen victories and seven defeats. Both leagues in which they have competed have resulted in ties. At this time the

players and rooters are at top pitch in anticipation of the play-offs in these circuits. Track work will start in the very near future, and we have very promising material for this spring sport. Now that ground is broken for our new building, we are looking forward to the prospect of our own gymnasium and anticipate even better basket-ball seasons than this year's.

The Dramatic Club of P. C. P. & S. has been quite active, having presented two sketches, both of which have been very much enjoyed by the student body and faculty. The activities of the dramatic club seem to be bringing the student body more closely together. On March 16th a short college skit was presented entitled "Gassed," and directed by Mrs. Ada S. Capwell, librarian of the college. Those in the cast were I. H. Burnett, C. F. Riley, I. Kurland and T. O. W. and C. A. Smith.

The Pharmascope has been quite successful this year and is proving a popular news item. It has been much improved under the direction of Mr. Arthur Osol, of the Bachelor of Science student group.

Dean Charles H. LaWall is away on a much-needed vacation tour through the West. Although we miss his energetic spirit and stimulating influence, we know that he deserves a pleasant respite after nearly thirty years of work at the college, during which time he has never been away from his desk for any length of time. Professor LaWall has just completed a tremendous task in the compiling of a rather unique book, "Four Thousand Years of Pharmacy," a history of the growth of Pharmacy from its earliest days to the modern times. This book is written in a popular style and can be enjoyed by all who are interested in knowing of the activities and progress in the scientific world. Of course anyone directly connected with the profession of Pharmacy should not be without this highly informative and at the same time easily readable volume. The book is published by Lippincott & Company.

Professor Ivor Griffith, Assistant Professor of Pharmacy, who is conducting Dean LaWall's lecture work in his absence, was the principal speaker recently at a celebration of St. David's Day, the Welsh National Holiday, which celebration was held at Bangor, Pennsylvania.

Professor Ivor Griffith gave a most interesting address on "Industrial Alcohol," at the Annual Philadelphia Drug Exchange dinner, given at the Benjamin Franklin Hotel March 16th.

The class in Botany visited Horticultural Hall in Fairmount Park for the purpose of identifying the various botanical specimens about which they had been studying.

American Pharmaceutical Association Headquarters Building Vote.—The following cities have received the highest vote in the order named in the first vote on the location of the Headquarters Building of the American Pharmaceutical Association:

Washington, D. C.; Chicago, Ill.; Cincinnati, Ohio; St. Louis, Mo.; Madison, Wis.

BOOK REVIEWS

Quantitative Analysis. Second Edition. By Stephen Popoff. P. Blakiston's Sons & Co., Philadelphia, 1927. Bound in cloth, 559 pages, 68 illustrations. $4.00.

A book worthy of attention from teachers of chemistry, students and laboratory technicians. It is arranged in five parts which are subdivided into chapters arbitrarily classified to indicate use for beginning students, advanced students, and for graduate students or teachers.

The first part is devoted to laboratory technic, description of apparatus giving its use and construction and special features of apparatus and materials. Then come the actual determinations in simple volumetric and gravimetric analysis which gradually develop the skill of the student as the exercises proceed.

The second part outlines calculations. Two chapters are given to the discussion of errors, classified as personal, instrumental, and errors of method. This section also includes oxidation and reduction reactions along with other subject matter.

Part three links up practice with theory which aids the student considerably and at the same time develops an appreciation for doing and knowing. In writing a text of quantitative analysis it is a personal matter as to what should be included or omitted; however, the chapters in this part are valuable in their consideration.

In this day of pH values at every turn, part four will be in demand by students and by men who have been graduated and are anxious for a working knowledge of the subject. Under electrometric titrations, description of apparatus, preparation of reagents, assembling of parts, directions for manipulation, illustrations of calculations, and numerous experiments in preparation and titration are given.

Few books up to this time give detailed directions for the actual manipulation of this class of apparatus. In this book, however, is given information that will give the worker a strong grasp of the subject.

Part five is an appendix of selected tables useful in the laboratory, including a table of five-place logarithms.

The book is illustrated with a few cuts of apparatus and several diagrams. The chapters end with problems while throughout the book many references are given on the subject matter. It is a good book of technical chemistry.

PAUL Q. CARD.

TRAVAUX DES LABORATORIES DE MATIÈRE MÉDICALE ET DE PHARMACIE GALÉNIQUE DE LA FACULTÉ DE PHARMACIE DE PARIS. Edited by Em. Perrot and Alb. Goris. Vol. 17, 1926. 8 vo., numerous illustrations. Vigot freres, Paris, 50 francs.

This valuable and interesting volume contains eight essays on important drugs, giving extensive information concerning the pharmacology, pharmacognosy, histology and chemistry of them. It is divided into six parts which are indicated by colored leaves and separately paged. The latter makes it impossible to give the total pages without addition but it is about seven hundred.

The most important and interesting essays are those on the Cinchonas and *Echinocactus williamsii* Lem., the plant that yields the "mescal button." This latter essay covers over three hundred pages and is comprehensive in its discussion of the subject. The article on the Cinchonas gives a rather full acount of the history of the discovery and introduction of the plant into medical use. As is generally known to physicians and pharmacists, the illness of the Countess del Chinchon, wife of Don Jeromino Fernandez de Cabrera Borodella y Mendoza (Viceroy at Loxa in Peru from 1629 to 1639) was treated satisfactorily by the use of a cinchona bark, which was

received from one of the aborigines. The author of the essay (Rouhier) thinks that the natives were not aware of the value of the bark, and that the Jesuit priests were the real discoverers. At any rate it is certain that the cinchona trees, growing wild on the slopes of the Andes, have given to the world one of its most valuable drugs. It is said that Alexander the Great died of malarial fever. How tremendously the world's history might have been changed if that forceful character had been preserved to a much longer life. It is stated that the word "kina" means "bark" in the original language. The use of cinchona was not at once unanimously approved, but its evident efficiency in all forms of malarial fever and the extensive occurrence of these diseases, made it one of the most prominent of drugs. The danger of the exhaustion of the plants in their native region gave rise to the successful methods of extensive cultivation. This phase of cinchona production is given considerable attention in the essay.

Among other contributions of moderate extent are an essay on Chaulmoogra seeds and other seeds that may be used in leprosy and a study of drying oils, often erroneously called "wood oils," both of which are by Perrot. An essay by Choquette follows on *Dirca palustris,* a tree known in Canada as "lead wood."

As noted above the most extensive essay in the volume is that on the species of cactus that yields the mescal button. This is by A. Rouhier. The plant is known to the aborigines as "peyotl." We could hardly expect a more comprehensive and detailed treatment of any plant than is given in this essay. Not only are the botanical relations and structure presented, but the ecology, uses and popular names are also enumerated. The tribal uses of the mescal button are described in much detail, even the musical notation of the chants being transcribed. The essay constitutes a volume in itself and after perusing it the investigator interested in the nature, source, character and effects of the mescal button will need no further information.

In the concluding part of the volume Perrot contributes an article on Pyrethrum, its preparations and falsifications, and, in association with Rouhier, a paper on "Yocco," a new source of caffeine.

The final essay is on the cinchona extracts of the French Pharmacopeia.

The volume is one of the most interesting and valuable contributions to practical pharmacology that has appeared anywhere of late. It is a model for other institutions to "go and do likewise."

The many full page half-tone illustrations are excellently shown on a somewhat light-weight paper. The separate paging of each essay makes reference slightly troublesome. The object was probably to afford to each author a reprint in correct paging, but this is really a minor matter. There is no index and only a brief table of contents without, of course, page indication, but the more extensive papers have summaries with pages noted. The volume represents very extensive labor in laboratory research and in consultation of the literature of the several subjects. It will be a welcome addition to any pharmaceutical library.

HENRY LEFFMANN.

The World Book Company, Yonkers-on-Hudson, N. Y., submitted the two following books belonging to the New-World Science Series, for review.

INTRODUCTORY COLLEGE CHEMISTRY. By Neil E. Gordon, Professor of Chemistry, University of Maryland. 12 mo., 687 pp. Illustrated. Cloth, $3.80.

This text is the outgrowth of a course given by the author to his classes and includes that body of facts, experiments and principles generally accepted as the basis for a beginning college course. The two distinctive features of the book are the following:

1. Our newer knowledge of the structure and nature of matter is applied in explanation of the facts of chemistry.
2. Our newer knowledge of educational principles and methods is applied in the organization and presentation of the material.

The volume is divided into two parts. Part I deals with Non-Metals and contains ten so-called books. Part II comprises Metals with eight books. The Appendix consists of Densities and Melting Points of the Elements, Weight and Solubility of Gases, Water Pressures of Water in Millimeters of Mercury and International Atomic Weights.

This valuable textbook can be used with profit in our colleges of pharmacy.

OTTO RAUBENHEIMER, Ph. M.

QUALITATIVE ANALYSIS. By William C. Cooper, M. S., Ph. D., Professor of Chemistry, DePaul University, Chicago. 12 mo., 142 pp. Cloth, $1.52.

The alchemists got results sometimes, but they did not know why and for that very reason consistent progress in their art was impossible. If students of chemistry do not grasp the theories that underlie the experiments, they might just as well learn so many tricks of alchemy. Frequently, very frequently, current textbooks on analysis prescribe methods for attaining results, without adequate explanation. In Professor Cooper's text on Qualitative Analysis the chief object has been to explain every step that is prescribed, giving reasons, to the end that students may become scientists and not empiricists, chemists and not alchemists.

The referee can only speak words of praise of this book.

OTTO RAUBENHEIMER, Ph. M.

A NATURALIST AT THE ZOO. By E. G. Boulenger. 206 pp. Brentano's, 1 W. 47 St., New York City.

Boulenger, a well-known naturalist and author of "The Aquarium Book," presents in the volume before us some of the inmates in the Zoological Garden of Regent's Park, London. He gives us interesting and amusing inside information about the history, habits and dispositions of the most popular as well as the most peculiar inhabitants of the Zoo. The numerous illustrations are taken from life and are by L. R. Brightwell.

We can highly recommend this book to pharmacists, quite especially as the study of zoology is usually neglected in their education.

OTTO RAUBENHEIMER, Ph. M.